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13. ABSTRACT *(Maximum 200 words)*

THIS REPORT IS A DETAILED DISCUSSION OF THE EVALUATIONS PERFORMED TO DEVELOP THE TOXICITY ASSESSMENT FOR RMA CONTAMINANTS IN SOIL. THE OBJECTIVES OF THE TOXICITY ASSESSMENT ARE TO:

1. DETERMINE THE NATURE AND EXTENT OF HEALTH AND ENVIRONMENTAL HAZARDS ASSOCIATED WITH EXPOSURE TO CONTAMINANTS PRESENT AT THE SITE
2. IDENTIFY A QUANTITATIVE INDEX OF TOXICITY FOR EACH TARGET CONTAMINANT, REFERRED TO IN THIS ASSESSMENT AS DT.

THE TOXICITY ASSESSMENT FOR THE RMA TARGET CONTAMINANTS HAS BEEN PERFORMED CONSISTENT WITH PUBLISHED EPA GUIDELINES AND ADDRESSES ONLY HUMAN HEALTH HAZARDS ASSOCIATED WITH CONTAMINANTS IN SOIL.

EACH TOXICITY PROFILE IS COMPOSED OF SEVEN SECTIONS:

1. SUMMARY
2. CHEMICAL AND PHYSICAL PROPERTIES
3. TRANSPORT AND FATE

14. SUBJECT TERMS
SOIL, HEALTH EFFECTS, EXPOSURE ASSESSMENT, WILDLIFE

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ROCKY MOUNTAIN ARSENAL

DRAFT FINAL REPORT

TOXICITY ASSESSMENT FOR
RMA TARGET CONTAMINANTS
VOLUME II

JUNE 1987
TASK ORDER 35

ENDANGERMENT ASSESSMENT RMA
CONTRACT NO. DAAK11-84-D-0017,

EBASCO SERVICES INCORPORATED
R.L. STOLLAR AND ASSOCIATES
CALIFORNIA ANALYTICAL LABORATORIES, INC.
UBTL INC. TECHNOS INC. GERAGHTY & MILLER, INC.

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PREPARED FOR

**PROGRAM MANAGER'S
OFFICE FOR
ROCKY MOUNTAIN ARSENAL CLEANUP**

US ARMY AMC

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Prepared by

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Prepared for

U.S. Army Program Manager's Office for
Rocky Mountain Arsenal Clean Up

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VOLUME II

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APPENDIX B - TOXICITY PROFILES

FLUORIDE[1/]

Summary

Small amounts of fluoride in ingested water and beverages have a beneficial effect on the prevention of dental caries, particularly among children. Chronic toxic effects of fluoride exposure include mottling of tooth enamel or dental fluorosis and skeletal fluorosis. Intake of fluoride for long periods in amounts greater than 20-40 mg/day may results in crippling skeletal fluorosis (NAS 1977). Reported adverse health effects following intake of milligram per liter levels of fluoride in drinking water including mongolism, cancer, mortality and mutagenic birth defects are unconfirmed (NAS, 1977).

Fluoride is commonly found in association with other elements; therefore the chemical and physical data presented under Chemical and Physical Properties is for a common fluoride compound, sodium fluoride. Physical/chemical data for other fluoride compounds will be different.

CAS Number: 16984-48-8

Chemical Formula: F^-

IUPAC Name: Fluoride

1/ Compiled from: United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL). 1985. Physical, Chemical, and Toxicological Data Summaries of 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

Also: Berkowitz, J.G., Goyer, M.M., Harris, J.C., Lyman, W.J., Horne, R.A., Nelten, L.H., Harrison, J.E., and Rosenblatt, D.H. 1978. Literature Review--Problem definition studies on selected chemicals. Final Report. Vol. III. Chemistry, toxicology, and potential environmental effects of selected organic pollutants. Contract No. DAMD 17-77-C-7037, Arthur D. Little, Inc. Cambridge, MA (AD B052946L).

Important Synonyms and Trade Names; Fluoride (1-), Fluoride ion

Chemical and Physical Properties

Molecular Weight: 41.99

Boiling Point: 1,704°C (Merck 1983)

Melting Point: 993°C (Merck 1983)

Specific Gravity: 2.78 (Merck 1983)

Solubility in Water: 4,300 mg/liter at 25°C (Merck 1983)

Solubility in Organics: Not soluble in alcohol (Merck 1983)

Transport and Fate

Fluorides pass both to and from the atmosphere, hydrosphere, lithosphere and biosphere in a continuous cycle (Berkowitz et al. 1978). The sources of fluorides are both natural and anthropogenic and include volcanism, entrainment of soil particles by wind and industrial emissions. A majority of these fluorides are transferred back to the earth by wet and dry deposition. In the atmosphere, many inorganic fluoride compounds are hydrolyzed rapidly by water vapor to less volatile compounds. Following reactions with water vapor, anhydrous hydrogen fluoride--an industrial pollutant--yields hydrofluoric acid. Elemental fluorine and halogen fluorides combine with water to form hydrogen fluoride and oxygen (Berkowitz et al. 1978).

Fluoride is commonly found in soils due to its presence as a constituent in a number of abundant minerals. Berkowitz et al. (1978) cite background fluoride levels of 290 ppm in the earth's crust, 715 ppm in igneous rocks, 220 ppm in sandstone, and 560 ppm in shale. A range of 100-300 ppm fluoride is typically found in many soils. A

large fraction of natural fluoride in soils is bound to soil particles; however, the amount may vary somewhat with the soils clay content, calcium carbonate content and pH (Berkowitz et al. 1978--Cite: Gisiger 1968). Many fluoride-containing minerals do exhibit some degree of water solubility and may be a source of fluoride input to groundwaters. The higher fluoride contents of unpolluted soils found a few feet below the soil surface indicate the mobility of the soluble fractions. In aqueous solution, the predominant form of fluoride is the fluoride ion (F^-), however other forms are possible. In salt water systems (oceans) which contain an average of 1.2-1.4 ppm F- (Berkowitz et al. 1978) approximately half is in the simple ion form while the majority of the remaining fluoride is in the complex ion form of insoluble magnesium fluoride.

The availability of fluoride for uptake by plants varies with soil conditions. Soil chemistry may also influence the toxicity of fluorides to plants. For example, the availability of fluoride is higher in sandy, acidic or carbonate rich soils than in clay rich or carbonate poor soils (Berkowitz et al. 1978 cite Bisiger 1968).

Fluorides are easily transferred through most food chains, however knowledge on the extent of biomagnification is lacking. Berkowitz et al. (1978) summarize fluoride tissue levels for a variety of animals and exposure scenarios. Oysters displayed bioconcentrations factors in their soft tissues ranging between 2 and 8 following exposure to increasing fluoride concentrations in seawater for 60 days, while prawns exhibited bioconcentration factors of 356 following exposure to 1.05 ppm F- in seawater for 72 days.

Health Effects

Humans ingesting water at optimal concentrations of fluoride for the prevention of dental caries do not appear to suffer adverse health effects. Acute fluoride toxicity is rare and usually due to accidental poisoning (Berkowitz et al. 1978). Symptoms include restlessness,

stiffness, anorexia, excessive salivation, nausea, vomiting, abdominal pain, chronic convulsions, depression and death, usually due to cardiac failure.

Prolonged (chronic) ingestion of elevated levels of fluoride is characterized by dental lesions (i.e., mottling of dental enamel) and skeletal fluorosis. Tooth discoloration can occur at concentrations of fluoride exceeding 2 ppm in water (Berkowitz et al. 1978). Skeletal fluorosis is often asymptomatic until the disease advances to the crippling stage. Symptoms of preskeletal fluorosis include pruritus (severe itching), excessive thirst, severe chronic fatigue and gastrointestinal upset.

Acutely high doses of sodium fluoride in male rats (50 mg/kg) resulted in an increased urinary excretion of inorganic phosphate, calcium, magnesium, potassium and sodium associated with an excessive secretion of urine (Berkowitz et al. 1978--Cite: Suketa and Mikami 1977). In other animal studies, male rats injected intraperitoneally with 35 mg/kg sodium fluoride exhibited kidney calcium levels 10 times that of controls and slightly elevated (1.5 times) levels of magnesium (Berkowitz et al. 1978--Cite: Suketa et al. 1977). Dose dependent hyperglycemia was also apparent in these rats.

Effects of fluoride on reproduction in rats and mice have been reported. Female mice raised on 50, 100 or 200 ppm sodium fluoride exhibited retarded growth and impaired reproduction at the two highest doses; half of the animals in the high dose group died within five weeks. Mice on the low dose regime showed declines in litter production though other aspects of reproduction were not influenced (Berkowitz et al. 1978--Cite: Messer et al. 1973).

Data on the mutagenicity of fluoride (Mohamed and Chandler 1976) are inconclusive due to inconsistencies in the experimental protocol. No information on the potential carcinogenicity of inorganic fluorides was located in the available literature.

The acute oral LD_{50} values of sodium fluoride in 30-, 45-, and 90-day-old rats are 54, 52, and 31 mg/kg, respectively. The greater resistance of the 30- and 45-day-old animals may reflect the greater efficiency of the younger skeletal systems in removing fluoride from circulation (Berkowitz et al. 1978).

Toxicity to Wildlife and Domestic Animals

Herbivorous dairy cattle may ingest fluoride through their intake of contaminated forage. Acute fluorine toxicosis in livestock generally occurs with intakes of greater than 250 ppm fluoride (Berkowitz et al. 1978). Symptoms of acute fluoride toxicosis include increased levels of fluoride in the blood and urine, stiffness, anorexia, reduced milk production, excessive salivation, nausea, vomiting, incontinence, chronic convulsions and cardiac failure. Chronic fluoride toxicosis is characterized by mottled teeth, lameness and abnormal levels of fluoride in bones and urine (Berkowitz et al. 1978).

Poultry may be more able to tolerate greater levels of fluoride than mammals (Berkowitz et al. 1978). Data on fluoride levels in chickens indicate that growing chicks can tolerate 300 ppm fluoride in their diet, while laying hens can tolerate up to 400 ppm (Berkowitz et al. 1978--Cite: NRC, 1977). Ducks ingesting dietary sodium fluoride at 4,220 ppm exhibited decreased growth but no mortality.

The acute toxicities of fluoride to a variety of fish species are summarized by Berkowitz et al. (1978): Rainbow trout, 5.9-7.5 ppm (LD_{50}) at 7.2°C (softened water); brown trout fry, 15-20 ppm (100 hr LC_{50}) at 12°C (softened water); rainbow trout, 2.7-4.7 ppm (48-240 hr LC_{50}) at 13°C; carp, 75-91 ppm (460 hr LC_{50}) at 20-24°C (softened water) and mosquito fish, 925 ppm (96-hour LC_{50}).

Regulations and Standards

National Primary Drinking Water Standard (USEPA): 4.0 mg/liter (MCL; 40 CFR 141.11)

OSHA Standards: TWA[1/] = 2.5 mg/m^3 (as F)

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

For fluoride the D_T value is based on the same data used by EPA to compute the current Risk Reference Dose (RfD) (USEPA 1986). The RfD is based on a study of children consuming fluoride in their drinking water at levels ranging from 0-14 ppm (Hodge 1950). Dental mottling was the endpoint of interest. A No-Observed-Adverse-Effect-Level (NOAEL) of 1 mg/liter (1 ppm) was identified from this study. In computing the RfD in mg/kg/day EPA assumed a 20 kg bodyweight as the children studied were between 12 and 14 years of age, and a water consumption rate of 1 liter/day. EPA also assumes that a 20 kg child consumes 0.01 mg/kg/day fluoride in the diet without an adverse effect (50 Federal Register 20164, Tuesday May 14, 1985). An Uncertainty Factor (UF) was not deemed necessary by EPA as the NOAEL is already determined for a sensitive population (i.e., children) and for a length of exposure that encompasses the critical toxic effect (USEPA 1986). Therefore a UF of 1 is used in computing the RfD (D_T). Derivation of the D_T for fluoride includes exposure from both drinking water and dietary exposure and is computed as follows:

1/ Time Weighted Average

$$D_T = \frac{\text{NOAEL (mg/kg/day)}}{\text{UF}} + \text{Dietary Intake}$$

$$= \frac{0.05}{1} + 0.01$$

$$= 0.05 \text{ mg/kg/day (water)} + 0.01 \text{ mg/kg/day (diet)}$$

$$= 0.06 \text{ mg/kg/day}$$

REFERENCES

BERKOWITZ, J.G., GOYER, M.M., HARRIS, J.C., LYMAN, W.J., HORNE, R.A., NELTEN, L.H., HARRISON, J.E., and ROSENBLATT, D.H. 1978. Literature Review--Problem definition studies on selected chemicals. Final Report. Vol. III. Chemistry, toxicology, and potential environmental effects of selected organic pollutants. Contract No. DAMD 17-77-C-7037, Arthur D. Little, Inc. Cambridge, MA (AD B052946L).

GISIGER, L. 1968. The Solubility of Various Fluorine Compounds in Soil. Fluoride Q. Rep., 1(1):21-26.

HODGE, H.C. 1950. The Concentration of Fluorides in Drinking Water to Give the Point of Minimum Caries with Maximum Safety. J. Am. Dent. Assoc., 40:436.

MESSER, H.H., ARMSTRONG, W.D., and SINGER, L. 1973. Influence of Fluoride Intake on Reproduction in Mice. J. Nutr., 103:1319-1326.

MOHAMED, A.H. and CHANDLER, M.E.W. 1976. Cytological Effects of Sodium Fluoride on Mitotic and Meiotic Chromosomes in Mice. Manuscript in Preparation.

NATIONAL ACADEMY OF SCIENCE (NAS). 1977. Drinking Water and Health. Volume I. National Academy of Sciences, Washington, DC. pg. 434.

NATIONAL RESEARCH COUNCIL (NRC). 1977. Effects of Fluorides in Animals. National Academy of Sciences, Washington, D.C.

SUKETA, Y. and MIKAMI, E. 1977. Changes in Urinary Ion Excretion and Related Renal Enzyme Activities in Fluoride-Treated Rats. Toxicol. Appl. Pharmacol., 40:551-559.

SUKETA, Y. and MIKAMI, E., and HAYASHI, M. 1977. Changes in Calcium and Magnesium in the Kidneys of Rats Intoxicated with a Single Large Dose of Fluoride. Toxicol. Appl. Pharmacol., 39: 313-319.

THE MERCK INDEX. 1983. An Encyclopedia of Chemicals, Drugs and Biologicals. Tenth ed. Windholz, M., Budavan, S., Blumetti, R.F. and Otterbein, E.S. (eds.). Merck and Company, Inc., Rahway, New Jersey.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1986. Risk Reference Dose for Fluoride. Integrated Risk Information System (IRIS). [Note: This is an EPA computerized data base.]

FLUOROACETIC ACID[1/]

Summary

Fluoracetic acid and its sodium salt, sodium fluoroacetate are acutely toxic to birds and mammals. Fluoroacetate is used primarily as a rodenticide and is toxic as a result of its oxidative conversion to fluorocitrate *in vivo*. Fluorocitrate effectively blocks the tricarboxylic acid cycle which is an essential mechanism in mammals for energy production. Data on the environmental persistence of fluoroacetate are lacking.

CAS Number: 144-49-0

Chemical Formula: CH_2FCOOH

IUPAC Name: 2-Fluoroacetic Acid

Important Synonyms and Trade Names: Fluoroethanoic Acid; Gifblaar Poison; MFA; Monofluoroacetic Acid.

Chemical and Physical Properties

Molecular Weight: 78.04 (Merck 1983)

Boiling Point: 165°C (Sax 1979)

Melting Point: 33°C (Merck 1983)

Specific Gravity: 1.369 (USEPA 1985)

1/ Compiled From: Various sources cited in the text and the bibliography.

Solubility in Water: Soluble (Merck 1983)

Solubility in Organics: Slightly soluble in petroleum ether

Log Octanol/Water Partition Coefficient (K_{ow}): Not Located

Soil/Water Partition Coefficient (K_{oc}): Not Applicable

Bioconcentration Factor: Not Applicable

Vapor Pressure: Not located.

Henry's Law Constant: Not Applicable

Transport and Fate

Scant information is available on the transport and fate processes of fluoroacetic acid or its sodium salt, sodium fluoroacetate. Both the acid and the salt are water soluble (USEPA 1985; Gosselin 1976). Sodium fluoroacetate is also nonvolatile (Gosselin 1976) and therefore, losses from environmental media due to evaporation would not be expected to occur. Under normal conditions of pH in soil and water it is likely that the compound will be present as a salt rather than as a free acid. Potassium fluoroacetate is a natural toxic constituent of the South African plant Dichaepetalum cymosum (Peters et al. 1981). Fluoroacetate is also a natural constituent of some poisonous plants, notably Acacia georginae, a perennial shrub found in Australia (Gosselin 1976). Neither plant is likely to occur naturally in the United States.

No data on the stability of fluoroacetic acid (or its sodium salt) in air, soil, water or its potential for bioaccumulation were located in available literature. However, given the soluble nature of fluoroacetic acid and its sodium salts, bioconcentration would not be expected to occur.

Health Effects

Data presented are for sodium fluoroacetate, the salt of fluoroacetic acid. The fluoroacetate ion itself is not toxic, but is converted *in vivo* to fluorocitric acid (fluorocitrate), a potent inhibitor of the tricarboxylic acid cycle--an essential mechanism in energy production in mammalian cells (Gosselin et al. 1976). The block is a result of the inhibition of aconitase which regulates the conversion of citrate to isocitrate. The result is an accumulation of large quantities of citrate in the tissues (Cassarett and Doull, 1980). Because the metabolic lesion involves an inhibition of oxidative energy metabolism, the heart and the central nervous system are the critical areas affected (Cassarett and Doull 1980). Symptoms of poisonings include nausea, vomiting, cardiac irregularities cyanosis and convulsions. Death is usually the result of ventricular fibrillation or respiratory failure. The estimated lethal dose for humans ranges from 2 to 10 mg/kg (Cassarett and Doull 1980).

Species differences are reported in the types of symptoms which precede death. Dogs usually die of convulsions or respiratory failure; however, in man, monkeys, horses and rabbits, central nervous system effects are often incidental with the principal complication arising from ventricular fibrillation (Cassarett and Doull 1980).

Few data are available on the effects of chronic poisoning with sodium fluoroacetate, however, renal changes similar to nephrosis have occurred in rats administered acutely lethal or repeated sublethal injections of fluorocitrate (Gosselin 1976). In one reported case of chronic poisoning, a rabbit exterminator exposed repeatedly over a period of 10 years exhibited severe and progressive lesions of the renal tubular epithelium and milder hepatic neurologic and thyroid dysfunctions (Gosselin 1976).

No data on reproductive effects, teratogenicity, carcinogenicity, or mutagenicity of fluoroacetic acid or related compounds was located in available literature. The oral LD_{50} values in rats, mice and guinea pigs are 4.7 mg/kg, 7 mg/kg, and 0.47 mg/kg, respectively (NIOSH 1983).

Toxicity to Widlife and Domestic Animals

Some poikilothermic animals are reported to be resistant to fluoroacetate; notably, the S. African clawed toad (Xenopus laevis) and some fish such as the bass and the bream (Bauermeister et al. 1977). The intraperitoneal LD_{50} of fluoroacetate in rainbow trout (Salmo gairdneri) is 500 μmole/kg (Bauermeister et al. 1977).

Acute oral toxicities (LD_{50}) are presented below for a variety of species (Hudson et al. 1984).

Species	LD_{50} (mg/kg)
bullfrogs (Rana catesbeiana),	54.4 mg/kg
mallard ducks (Anas platyrhynchos),	9.11 mg/kg
golden eagles (Aquila chrysaetos)	3.54 mg/kg
California quail (Callipepla californica),	4.63 mg/kg
Japanese quail (Coturnix c. japonica),	12.8 mg/kg
ring-necked pheasant (Phasianus colchicus),	6.46 mg/kg
Chukar (Alectoris chukar),	3.51 mg/kg
turkeys (Meleagris gallopavo),	4.76 mg/kg
domestic pigeons (Columba livia)	4.24 mg/kg;
house sparrows (Passer domesticus)	3.0 mg/kg
domestic ferrets (Mustela putorius)	1.41 mg/kg
mule deer (Odocoileus h. hemionus)	0.33-1.0 mg/kg

Hudson et al. (1984) reported secondary toxicity in fasted ferrets fed live or dead mice previously dosed with 1, 2, 4, or 8 mg/kg sodium fluoroacetate. Only one ferret survived; this following the ingestion of one of two low-dose (2 mg/kg) mice.

Regulations and Standards

OSHA Permissible Exposure Limit: TWA[1/] = 0.05 mg/m^3 (sodium salt)

ACGIH Threshold Limit Value: TWA = 0.05 mg/m^3 (sodium salt)
STEL[2/] = 0.15 mg/m^3 (sodium salt)

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

For fluoroacetic acid, the D_T value is derived from an acute oral toxicity value (LD_{50}) in guinea pigs. The D_T is computed as the product of the acute value and an application factor of 1×10^{-5} (Layton et al., 1986). The application factor allows the derivation of an interim acceptable longterm intake rate (D_T) based on the results of acute tests (LD_{50}) in the absence of more suitable longterm studies (i.e., No-Observed-Effect-Level, NOEL, studies). The application factor corresponds to the cumulative percentile on a lognormal distribution of NOEL/LD_{50} ratios for various chemicals. The percentile was chosen to reduce the probability that the calculated dose rate would be above a toxic level; the 5th cumulative percentile was used by Layton et al. (1986) and was found to be equal to 10^{-3}. The application factor also includes a safety factor of 100 to address interspecies and intraspecies variability; therefore, an interim estimate of D_T is obtained when the application factor is multiplied by the acute value. Derivation of this D_T value is as follows:

$$D_T = \text{Acute oral } LD_{50} \times \text{Application Factor}$$
$$= 0.47 \text{ mg/kg/day} \times 1 \times 10^{-5}$$
$$= 0.0000047 \text{ mg/kg/day}$$

1/ Time Weighted Average.
2/ Short Term Exposure Level.

REFERENCES

AMERICAN CONFERENCE OF GOVERNMENTAL INDUSTRIAL HYGIENISTS (ACGIH). TLV Threshold Limit Values For Chemical Substances in Workroom Air Adopted by ACGIH for 1981. Cincinnati, OH.

BAUERMEISTER, A., THOMPSON, C.J. and NIMMO, I.A. 1977. The susceptibility of rainbow trout to fluoroacetate. Biochemical Society Transactions, 5(1);304-305.

CASARETT and DOULL'S TOXICOLOGY. 1980. The Basic Science of Poisons. Second Edition. Doull, J., Klaassen, C.D., and Amdur, M.O. (Editors). Macmillan Publishing Company, Inc., New York. 778 pp.

GOSSELIN, R.E. (Editor). 1976. Clinical Toxicology of Commercial Products. Fourth Edition. Section III, pp. 193-196. Williams and Wilkins, Baltimore, MD.

HUDSON, R.H., TUCKER, R.K. AND HAEGALE, M.A. 1984. Handbook of Toxicity of Pesticides to Wildlife. Second Edition. United States Department of the Interior Fish and Wildlife Service. Resource Publication 153. Washington, D.C. 1984.

LAYTON, D.W., MALLOU, B.J., ROSENBLATT, D.H. and SMALL, M.J. 1986. Deriving Allowable Daily Intakes For Systemic Toxicants Lacking Chronic Toxicity Data. Regulatory Toxicology and Pharmacology. In Press.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH). 1983. Registry of Toxic Effects of Chemical Substances. Volumes I-III. Department of Health and Human Services. Cincinnati, OH.

OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION (OSHA). 1984. Occupational Safety and Health Standards. Subpart Z. Toxic and Hazardous Substances. (29 CFR 1910.1000). pp. 660-665.

PETERS, R.A., H. SPENCER, and P.L. BIDSTRUP. 1981. Subacute Fluoroacetate Poisoning. Journal of Occupational Medicine. 23(2):112-113.

SAX, I.N. 1979. Dangerous Properties of Industrial Materials, Fiftn Edition. Van Nostrand Reinhold Company, New York.

THE MERCK INDEX. 1983. An Encyclopedia of Chemicals, Drugs and Biologicals. Tenth ed. Windholz, M., Budavan, S., Blumetti, R.F. and Otterbein, E.S. (eds.). Merck and Company, Inc., Rahway, New Jersey.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1985. Chemical Emergency Preparedness Program. Interim Guidance. Chemical Profiles. Office of Solid Waste and Emergency Response. USEPA Washington, D.C. Revision 1. 9223.0-1A. December 1985.

HEXACHLOROCYCLOPENTADIENE[1/]

Summary

Hexachlorocyclopentadiene (HCPD) has not presently been shown to be carcinogenic in animals or humans; however, The National Cancer Institute has selected HCPD for testing. No evidence of mutagenicity has been established for HCPD in either mammalian or bacterial test systems. In animals studies, HCPD given orally resulted in toxic nephrosis in female mice and in male and female rats. Rats exposed to high concentrations of HCPD via inhalation experienced mortality, depressed body weights, increased kidney weights (females only) and pulmonary degenerative changes. HCPD has not resulted in teratogenic or embryotoxic effects following its administration to rabbits and rats; however, maternal toxicity was observed in treated rabbits.

CAS Number: 77-47-4

Chemical Formula: C_5Cl_6

IUPAC Name: 1,2,3,4,5,5'-Hexachloro-1,3-cyclopentadiene

Important Synonyms and Trade Names: HCPD; Perchlorocyclopentadiene

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1/ Compiled from: United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL). 1985. Physical, Chemical, and Toxicological Data Summaries of 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

Also: U.S. Environmental Protection Agency (USEPA) 1984. Health Effects Assessment for Hexachlorocyclopentadiene. Environmental Criteria and Assessment Office, Office of Research and Development. Cincinnati, OH.

Chemical and Physical Properties

Molecular Weight: 273

Melting Point: -9.6°C (USEPA 1984)

Boiling Point: 239°C at 753 mm Hg (Hawley 1977; Stevens 1979)
234°C (Irish 1963)

Specific Gravity: 1.715 at 15.5°C (Hawley 1977)

Solubility in Organic Solvents: Miscible in hexane (Bell et al. 1978)

Solubility in Water: 2.1 mg/liter at 25°C (Dal Monte and Yu 1977)
1.8 mg/liter at 28°C (Wolfe et al. 1982)
0.805 mg/liter at 25°C (Lu et al. 1975)

Log Octanol/Water Partition Coefficient (K_{ow}): 3.52 (Lyman et al., 1982) Fragment Method
5.04 (Wolfe et al. 1982)

Soil/Water Partition Coefficients (K_{oc}):

1,304	Lyman et al. (1982) Eqn 4-5 (S = 9)
1,910; 12,500	Lyman et al. (1982) Eqn 4-8 (log K_{ow} = 3.5; 5)
1,540; 22,600	Lyman and Loreti (1986) Eqn I (log K_{ow} = 3.5, 5)
1,640; 29,300	Lyman and Loreti (1986) Eqn II (log K_{ow} = 3.5, 5)
1,630; 28,054	Lyman and Loreti (1986) Eqn III (log K_{ow} = 3.5, 5)
2,050	Kadeg et al. (1986) (log K_{ow} = 3.5)
24,400	Kadeg et al. (1986) (log K_{ow} = 5)

Bioconcentration Factor:

29	Veith et al. (1979) (experimental)
11	ECAO 1980
279	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 3.52)
195	Davies and Dobbs (1984) Eqn B (log K_{ow} = 3.52)
107.6	Davies and Dobbs (1984) Eqn C (log K_{ow} = 3.52)
179	Davies and Dobbs (1984) Eqn A (S = 9)
717	Davies and Dobbs (1984) Eqn C (log K_{ow} = 5.04)
1,570	Davies and Dobbs (1984) Eqn B (log K_{ow} = 5.04)
3,980	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 5.04)

Vapor Pressure: 0.08 mm Hg at 25°C (Irish 1963)
0.975 mm Hg at 62°C (Stevens 1979)

Henry's Law Constant: 0.0137 atm-m^3/mole (USEPA 1985)
0.027 atm-m^3/mole (Atallah et al. 1980; Wolfe et al., 1982)

Transport and Fate

Hexachlorocyclopentadiene (HCPD) is known to volatilize rapidly from water (USEPA 1984); however, it is not likely to persist following its release to air. The estimated tropospheric residence time (Cupitt 1980) is approximately five hours based on reactions with hydroxyl radicals and ozone (USEPA 1984). Atmospheric photolysis of HCPD is likely since HCPD has a chromophore which absorbs light in the solar spectrum. The degradation products are thought to be ClCO, diacylchlorides, ketone and free Cl radical (USEPA 1984).

HCPD is known to photolyze in aqueous media. In flowing bodies of water, photolysis, hydrolysis, volatilization and biodegradation will all contribute to the loss of HCPD. The photolytic half-life of HCPD in shallow water (<5 cm depth) is estimated to be 10 minutes (USEPA 1984). Hydrolysis is much slower with a half-life ranging from 3-11 days at pHs of 5-9 and temperatures between 25 and 30°C (Wolfe et al. 1982).

The fate and transport of HCPD in soils is affected by its strong tendency to adsorb onto organic matter (USEPA 1984). A range of estimated soil/water partition coefficients (K_{OC}) is reported above and indicates that sorption of HCPD to soils/sediments and dissolved organic material will occur. The combined low water solubility and high organic partitioning for HCPD suggests that this compound will not be an environmentally mobile contaminant. HCPD is known to be metabolized by a number of soil microorganisms (USEPA 1984).

A range of estimated and experimental bioconcentration factors (BCFs) for HCPD is also reported above. ASTM (1985) indicates that chemicals with bioconcentration factors less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the estimated concentration factors suggests that appreciable bioconcentration or biomagnification of HCPD residues would occur; however, experimental data appear to indicate that uptake is not considerable (USEPA 1984).

Health Effects

Little data is available on the health effects of HCPD exposures in humans. The compound is very irritating to the eyes and mucous membranes and induces lacrimation, sneezing and salivation. Repeated contact with the skin causes blistering burns, and inhalation causes pulmonary edema (USEPA 1984).

Subchronic (90-day) oral exposures of mice to doses of HCPD (19, 38, 75, 150, 300 mg/kg) 5 days/week resulted in lesions of the forestomach in both sexes at 38 mg/kg (USEPA 1984). At the highest dose all male mice died by day 8 and 3 females by day 14. In female mice the liver was enlarged and toxic nephrosis was evident at doses greater than 75 mg/kg. In another phase of the study, rats were orally exposed to doses of 10, 19, 38, 75, and 150 mg/kg HCPD. Mortality and toxic nephrosis was observed in both males and females at doses >38 mg/kg (USEPA 1984). Female rats exposed to 19 mg/kg exhibited lesions of the forestomach. A dose-related depression in bodyweight gain was also observed relative to controls.

Rats and monkeys exposed subchronically (14 weeks) to HCPD via inhalation at doses of 0, 0.1, 0.05 and 0.20 ppm exhibited no treatment related abnormalties in gross pathology, histopathology, hematology, or clinical chemistry. However, slight but statistically insignificant increases in hemoglobin concentration and erythrocyte counts were seen in the 0.01 ppm and 0.20 ppm male rats and the 0.05 ppm female rats (USEPA 1984).

Male and female rats chronically exposed (30 weeks) via inhalation to doses of 0, 0.05, 0.1, and 0.5 ppm HCPD 6 hours/day, 5 days/week exhibited a number of effects (USEPA 1984). At the highest dose level, mortalities of males and females occurred. Males in this dose group exhibited depressed weight gain following the seventh week of exposure and for the remainder of the study. Females in the medium and high dose groups also exhibited depressed body weights. Pulmonary, kidney and liver degenerative changes were observed in both sexes at the high dose. Kidney weights of high dose females were significantly increased.

No reproductive impairment or evidence of teratogenicity was observed in pregnant rats orally administered HCPD at doses of 3, 10 or 30 mg/kg/day during days 6-15 of gestation (USEPA 1984). No evidence of teratogenicity was apparent in mice or rabbits orally dosed with 0, 5, 25 or 75 mg/kg/day HCPD during days 6-15 (mice) of gestation (USEPA 1984). Fertility was not significantly different in either dosed mice or rabbits. No maternal toxicity or embryotoxicity occurred in treated mice; however, maternal toxicity did occur at 75 mg/kg/day in rabbits. No embryotoxic effects were noted at any dose level in rabbits (USEPA 1984).

No evidence of the carcinogenicity of HCPD has been demonstrated in animals or humans (USEPA 1984); however, the National Toxicology Program (NTP) is currently scheduled to start carcinogenicity testing in 1986 (NTP 1986). It has not been shown to be mutagenic in a variety of bacterial (E. Coli, S. typhinnurium) and mammalian cell cultures (mouse lymphoma). The acute oral LC_{50} of HCPD in rats ranges from 500-630 mg/kg (USEPA 1980).

Toxicity to Wildlife and Domestic Animals

Very little information is available on the toxicity of HCPD to wild and domestic animals. The acute oral LD_{50} of HCPD in rabbits ranges between 420 and 620 mg/kg (USEPA 1980). Freshwater and marine aquatic organisms exhibit acute toxic effects at concentrations of HCPD as low as 7 µg/liter; while freshwater organisms exhibit chronic effects at concentrations of 5 µg/liter (USEPA 1986a).

Regulations and Standards

Ambient Water Quality Criteria (USEPA 1986a):

The available data are not adequate for establishing criteria. However, EPA does report the lowest values known to be toxic in aquatic organisms.

Aquatic Life (Freshwater)

Acute Toxicity: 7 µg/liter
Chronic Toxicity: 5.2 µg/liter

Aquatic Life (Saltwater)

Acute Toxicity: 7 µg/liter
Chronic Toxicity: Data are insufficient

Human Health

Criterion: 206 µg/liter

ACGIH Threshold Limit Value (1980): 0.1 mg/m^3

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

For HCPD, the D_T value is based on the same data used by EPA to compute the current Risk Reference Dose (RfD) (USEPA 1986b). The RfD is based on a subchronic oral (gavage) toxicity study in which male and female rats were administered HCPD at doses of 0, 10, 19, 38, 75, or 150 mg/kg/day, 5 days/week for 13 weeks (Abdo et al. 1984). Stomach

lesions were observed in 2 of 8 surviving females at 19 mg/kg/day. An increased incidence and severity of effects was noted in both sexes at the higher doses, as well as an increased incidence of nephrotoxicity in females. The No-Observed-Adverse-Effect-Level (NOAEL) identified from this study was 7 mg/kg/day. [Note: EPA multiplies the actual NOAEL of 10 mg/kg/day by a conversion factor of 5/7 days to account for the less than continuous exposure duration in determining the final NOAEL level.] An Uncertainty Factor (UF) of 1,000 is included to address the extrapolation of results to humans (10), intraspecies variability (sensitive subgroups) (10) and to account for the use of a subchronic rather than a chronic experimental exposure (10). Derivation of the D_T value for HCPD is as follows:

$$D_T = \frac{\text{NOAEL (mg/kg/day)}}{\text{UF}}$$

$$= \frac{7}{1{,}000}$$

$$= 0.007 \text{ mg/kg/day}$$

REFERENCES

ABDO, K.M., MONTGOMERY, C.A., KLUWE, W.M. FARRELL, D.R. and PREJEAN, J.D. 1984. Toxicity of hexachlorocyclopentadiene: Subchronic (13-week) administration by gavage to F344 rats and B6C3F1 mice. J. Appl. Toxicol. 4:75-81.

ASTM. 1985. Standard Practice for conducting bioconcentration tests with fishes and saltwater bivalve mollusca. Designation E 1022-84, pages 590-62. In: 1985 Annual Book of ASTM Standards Volume 11.04. American Society for Testing and Materials, Philadelphia, Pennsylvania.

ATALLAH, Y.H, WHITACRE, D.M. and BUTZ, R.G. 1980. Fate of hexachlorocyclopentadiene in the environment. In: USEPA 1984. Health Effects Assessment for Hexachlorocyclopentadiene. Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office. Cincinatti, Ohio. EPA/540/1-86/001.

DAL MONTE, R.P. and YU, C.C. 1977. Water Solubility of MC-984 and Hex. Velsicol Chemical Corporation, Chicago, Illinois. In: USEPA 1984. Health Effects Assessment Document for Hexachlorocyclopentadiene. Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office. Cincinatti, Ohio. EPA 540/1-86/001.

DAVIES, R.P. and A.J. DOBBS. 1984. The prediction of bioconcentration in fish. Water Res. 18(10):1253-1262.

ECAO 1980 (see USEPA 1980).

HAWLEY, G.G (Editor). 1977. Condensed Chemical Dictionary. Nineth Edition. Van Nostrand, Reinhold Co. New York.

IRISH, D.D. 1963. Halogenated Hydrogenated Hydrocarbons: II. Cyclic. Hexachlorocyclopentadiene. In: Industrial Hygiene and Toxicology, Second Revised Edition. F.A. Patty (Ed.) John wiley and Sons, Inc. New York. p. 1333-1363.

KADEG, R.D., PAVLOU, S.P., DUXBURY, A.S. 1986. Elaboration of Sediment Normalization Theory for Non Polar Hydrophobic Organic Chemicals. U.S. Environmental Protection Agency, Criteria and Standards Division, Washington D.C.

LU, P.Y., METCALF, R.L., HIRWE, A.S. AND WILLIAMS, J.W. 1975. Evaluation of environmental distribution and fate of hexachlorocyclopentadiene, chlordane, heptachlor and heptachlor expoxide in a laboratory model ecosystem. J. Agric. Food Chem. 23:967-973.

LYMAN, W.J., LORETI, C.P. 1986. Prediction of Soil and Sediment Sorption for Organic Compounds (Comment Final Draft). U.S. Environmental Protection Agency, Monitoring and Data Support Division, Office of Water Regulations and Standards. Washington D.C.

LYMAN, W.J., REEHL, W.F., and ROSENBLATT, D.H. 1982. Handbook of Chemical Property Estimation Methods: Environmental Behavior of Organic Compounds. McGraw-Hill Book, Co., New York, NY.

NATIONAL TOXICOLOGY PROGRAM (NTP). 1986. Fiscal Year 1986 Annual Plan. U.S. Department of Health and Human Services. Public Health Service. Washington, D.C. NTP-86-086. May 1986.

STEVENS, J.E. 1979. Chlorinated derivatives of cyclopentadiene. In: USEPA 1984. Health Effects Assessment for Hexachlorocyclopentadiene. Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office. Cincinatti, Ohio. EPA/540/1-86/001.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1986a. Quality Criteria for Water, 1986 ("The Gold Book"). Office of Water Regulations and Standards, Washington, DC. EPA 440/5-86-001.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1986b. Risk Reference Dose for Hexachlorocyclopentadiene. Integrated Risk Information System (IRIS). [Note: This is an EPA computerized database.]

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1985. Draft Superfund Public Health Evaluation Manual. Prepared by: ICF Incorporated, Washington, D.C. USEPA Office of Solid Waste and Emergency Response, Washington, D.C. EPA Contract No. 68-01-7090.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1984. Health Assessment Document for Hexachlorocyclopentadiene. Final Report. Office of Health and Environmental Assessment. Washington, D.C. EPA-600/8-84-001F.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1980. Ambient Water Quality Criteria for Hexachlorocyclopentadiene. Environmental Criteria and Assessment Office. Cincinatti, Ohio. 440/5-80-055.

VEITH, G.D., DEFOE, D.C., and BERGSTEDT, B.V. 1979. Measuring and estimating bioconcentration factor of chemicals in fish. J. Fish. Res. Board Can. 36:1040-1048. In: USEPA 1984.

WOLFE, N.L., ZEPP, R.G., SCHLOTZHAVER, P. and SINK, M. 1982. Transformation pathways of hexachlorocyclopentadiene in the aquatic environment. Chemosphere. 11(2):91-101.

ISODRIN[1/]

Summary

No data on the carcinogenicity, teratogenicity, mutagenicity, chronic toxicity or reproductive toxicity of isodrin were located in available literature for animals or humans. The acute oral toxicity of isodrin in young rats (90 days of age) was 7 mg/kg.

CAS Number: 465-73-6

Chemical Formula: $C_{12}H_8Cl_6$

IUPAC Name: 1,2,3,4,10,10-hexachloro-1,4,4a,5,8,8a-hexahydro-1,4,5,8-endo-endo-dimethanonaphthalene

Important Synonyms and Trade Names: Isodrin; Compound 711

Chemical and Physical Properties

Molecular Weight: 365

Melting Point: 240-242°C (Merck 1983)

Solubility in Water: 0.16 mg/liter (Lyman et al. 1982) Estimated

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1/ Compiled from: United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL). 1985. Physical, Chemical, and Toxicological Data Summaries of 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

Also: Berkowitz, J.G., Goyer, M.M., Harris, J.C., Lyman, W.J., Horne, R.A., Nelten, L.H., Harrison, J.E., and Rosenblatt, D.H. 1978. Literature Review--Problem definition studies on selected chemicals. Final Report. Vol. II. Chemistry, toxicology, and potential environmental effects of selected organic pollutants. Contract No. DAMD 17-77-C-7037, Arthur D. Little, Inc. Cambridge, MA (AD B052946L).

Log Octanol/Water Partition Coefficient (K_{ow}):

6.51 (Lyman et al. 1982) Fragment Method

Soil/Water Partition Coefficient (K_{oc}):

5,900; 93,800	Lyman et al. (1982) Eqn 4-8 (log K_{ow} = 4.4; 6.6)
3,560	Lyman et al. (1982) Eqn 4-5 (S = .16)
7,720; 399,000	Lyman and Loreti (1986) Eqn I (log K_{ow} = 4.4, 6.6)
9,260; 633,000	Lyman and Loreti (1986) Eqn II (log K_{ow} = 4.4, 6.6)
9,990; 8,990; 584,000	Lyman and Loreti (1986) Eqn III (log K_{ow} = 4.4, 6.6)
9,050; 342,100	Kadeg et al. (1986) (low K_{ow} = 4.4, 6.6)

Bioconcentration Factor:

11,708	Davies and Dobbs (1984) Eqn B (log K_{ow} = 6.5)
51,286	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 6.5)
4,436	Davies and Dobbs (1984) Eqn C (log K_{ow} = 6.5)
1,737	Davies and Dobbs (1984) Eqn A (S = .16)
233	Davies and Dobbs (1984) Eqn C (log K_{ow} = 4.38)
635	Davies and Dobbs (1984) Eqn B (log K_{ow} = 4.38)
1,260	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 4.38)

Vapor Pressure: $<1 \times 10^{-4}$ mm Hg [estimated for 25°C] (Cogley and Foy 1978)

Henry's Law Constant: 4.8×10^{-4} atm-m^3/mole (calculated)

Transport and Fate

Very little information is available on the fate and transport of isodrin under environmental conditions; indeed, the physical/chemical properties of this compound have not yet been fully characterized. Photodrin formation has been observed following reactions of isodrin with acid, bromine, hydrogen bromide and ultraviolet (UV) light in the laboratory (Berkowitz et al. 1978). However, under field conditions, photoconversion of isodrin to photodrin is not expected as the maximum UV absorption of isodrin (198 nm) occurs in a region of the atmosphere where solar radiation is attenuated by both the ozone layer and by water (Berkowitz et al. 1978).

Isodrin is estimated to have a very low vapor pressure and a relatively low solubility in water (Cogley and Foy 1978). Therefore, it appears reasonable to assume that volatilization of isodrin to air, and leaching of isodrin contaminated soil residues to groundwater will not occur to an appreciable extent. A range of estimated soil/water partition coefficients (K_{oc}) is reported above and indicates that sorption of isodrin to soils/sediments and dissolved organic material will occur. Pavlou (1980) estimates that sorption of chlorinated hydrocarbon pesticides is very high. The combined low estimated water solubility and high organic partitioning indicate that isodrin will exhibit little environmental mobility. The persistence of isodrin in various soils under varying experimental conditions, as summarized by Berkowitz et al. (1978), indicates that detectable residues may be present in excess of 13 years post-application.

No residues of isodrin were found in soybeans, corn or oats grown in soil treated with isodrin (Nash et al. 1973). Ten weeks following application of isodrin (0.19 ppm) to soils, up to three percent of the applied quantity was recovered unchanged in the leaves of exposed carrots while 41 percent remained unchanged in the soils (Berkowitz et al. 1978 cite Klein et al. 1973). Conversion products which accounted for a majority of the remaining residues were identified as endrin.

A range of estimated bioconcentration factors (BCFs) for isodrin is also reported above. ASTM (1985) indicates that chemicals with bioconcentration factors less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the concentration factors suggests that appreciable bioconcentration or biomagnification of isodrin residues can occur.

Health Effects

No information on the toxicity of isodrin to humans was located in available literature. Additionally, no data on the carcinogenicity, mutagenicity, subchronic, chronic or reproductive toxicity was available for animals in the literature reviewed. Only acute oral toxicity data are available for laboratory mice and rats. The LD_{50} values for these animals are 7-15.5 mg/kg for female and male rats (>90 days old); 16.4-27.8 mg/kg for young female and male rats (25-31 days old) and 8.8 mg/kg for mice (Berkowitz et al. 1978).

Toxicity to Wildlife and Domestic Animals

Limited data is available on the toxicity of isodrin in wild and domestic animals. The dermal LD_{50} in rabbits was estimated at <94 mg/kg (Berkowitz et al. 1978). Endrin, an isomer of isodrin, was consistently the most toxic chemical among 89 chemicals tested in bobwhite, pheasants, mallards and Japanese quail (Heath et al. 1972). Isodrin would therefore be expected to exhibit somewhat similar toxic properties.

Comparisons of the toxicities of isodrin and photodrin in fish to those of several other cyclodiene insecticides indicate that isodrin was more toxic (Berkowitz et al. 1978). Reported LC_{50} values for freshwater fish were 2.5 ppb, 6.0 ppb, 6.0 ppb and 1.5 ppb in bass, bluegill, golden shiners and goldfish, respectively (Berkowitz et al. 1978).

Regulations and Standards

None located.

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or

should not pose a risk of cancer occurrence greater than a predetermined risk level.

For isodrin, the D_T value is derived from an acute oral toxicity value (LD_{50}) in female rats. The D_T is computed as the product of the acute value and an application factor of 1×10^{-5} (Layton et al., 1986). The application factor allows the derivation of an interim acceptable longterm intake rate (D_T) based on the results of acute tests (LD_{50}) in the absence of more suitable longterm studies (i.e., No-Observed-Effect-Level, NOEL, studies). The application factor corresponds to the cumulative percentile on a lognormal distribution of $NOEL/LD_{50}$ ratios for various chemicals. The percentile was chosen to reduce the probability that the calculated dose rate would be above a toxic level; the 5th cumulative percentile was used by Layton et al. (1986) and was found to be equal to 10^{-3}. The application factor also includes a safety factor of 100 to address interspecies and intraspecies variability; therefore, an interim estimate of D_T is obtained when the application factor is multiplied by the acute value. Derivation of this D_T value is as follows:

$$D_T = \text{Acute oral } LD_{50} \times \text{Application Factor}$$

$$= 7.0 \text{ mg/kg/day} \times 1 \times 10^{-5}$$

$$= 0.00007 \text{ mg/kg/day}$$

REFERENCES

ASTM. 1985. Standard Practice for conducting bioconcentration tests with fishes and saltwater bivalve mollusca. Designation E 1022-84, pages 590-62. In: 1985 Annual Book of ASTM Standards Volume 11.04. American Society for Testing and Materials, Philadelphia, Pennsylvania.

BERKOWITZ, J.G., GOYER, M.M., HARRIS, J.C., LYMAN, W.J., HORNE, R.A., NELTEN, L.H., HARRISON, J.E., and ROSENBLATT, D.H. 1978. Literature Review--Problem definition studies on selected chemicals. Final Report. Vol. II. Chemistry, toxicology, and potential environmental effects of selected organic pollutants. Contract No. DAMD 17-77-C-7037, Arthur D. Little, Inc. Cambridge, MA (AD B052946L).

COGLEY, D.R. AND FOY, W. 1978. Readily Available Data on 169 Compounds Associated with Operations at Rocky Mountain and Pine Bluff Arsenals. United States Army Medical Research and Development Command, Ft. Detrick, Frederick, MD. December 1978. AD A074214.

DAVIES, R.P. and A.J. DOBBS. 1984. The prediction of bioconcentration in fish. Water Res. 18(10):1253-1262.

HEATH, R.G., SPANN, J.W., HILL, E.F. AND KREITZER, J.F. 1972. Comparative Dietary Toxicities of Pesticides to Birds. U.S. Dept. of Interior, Fish and Wildlife Service. Bureau of Sport Fisheries and Wildlife, Special Scientific Report -- Wildlife, No. 152, Washington, D.C.

KADEG, R.D., PAVLOU, S.P., DUXBURY, A.S. 1986. Elaboration of Sediment Normalization Theory for Non Polar Hydrophobic Organic Chemicals. U.S. Environmental Protection Agency, Criteria and Standards Division, Washington D.C.

KLEIN, W., ZARIF, S. AND WEISGERBER, I. 1973. Residual Behavior of Isodrin ^{14}C and its conversion products in white cabbage and carrots. Chem. Mikrobiol. Technol. Lebensm, 1:121-125. In: Berkowitz et al., 1978 (see reference above).

LAYTON, D.W., MALLOU, B.J., ROSENBLATT, D.H. and SMALL, M.J. 1986. Deriving Allowable Daily Intakes For Systemic Toxicants Lacking Chronic Toxicity Data. Regulatory Toxicology and Pharmacology. In Press.

LYMAN, W.J., LORETI, C.P. 1986. Prediction of Soil and Sediment Sorption for Organic Compounds (Comment Final Draft). U.S. Environmental Protection Agency, Monitoring and Data Support Division, Office of Water Regulations and Standards. Washington D.C.

LYMAN, W.J., W.F. REEHL AND D.H. ROSENBLATT. 1982. Handbook of Chemical Property Estimation Methods: Environmental Behavior of Organic Compounds. McGraw-Hill Book Co., New York, NY.

NASH, R.G., HARRIS, W.G., ENSOR, P.D. AND WOOLSON, E.A. 1973. Comparative extraction of chlorinated hydrocarbon insecticide from soils 20 years after treatment. J. Assoc. Offic. Agr. Chemists, 56(3):728-732.

PAVLOU, S.P. 1980. Thermodynamic Aspects of Equilibrium Sorption of Persistent Organic Molecules at the Sediment-Seawater Interface: A Framework For Predicting Distributions in the Aquatic Environment. IN: Contaminants and Sediments. Volume 2. Baker, R.A. (Editor). Science Publishers, Inc. Ann Arbor, MI.

THE MERCK INDEX. 1983. An Encyclopedia of Chemicals, Drugs and Biologicals. Tenth ed. Windholz, M., Budavan, S., Blumetti, R.F. and Otterbein, E.S. (eds.). Merck and Company, Inc., Rahway, New Jersey.

ISOPROPYLMETHYL PHOSPHONIC ACID/ISOPROPYLMETHYL PHOSPHONATE[1/] [2/]

Summary

In mice and rats the acute toxicity of sodium isopropylmethyl phosphonic acid (IMPA) is low. No data are available on the effects of long-term (chronic) exposures to IMPA in animals or humans. However, a subchronic study in rats indicated that 300 mg/kg was without effect following a 90-day experimental exposure. Sodium IMPA was not mutagenic in tests with Salmonella. No data are available on the carcinogenicity, teratogenicity or reproductive toxicity of IMPA.

CAS Number: 1832-54-8

Chemical Formula: $C_4H_{10}O_2P$

IUPAC Name: O-Isopropyl methylphosphonic acid

Important Synonyms and Trade Names: Isopropylmethyl phosphonate; IMP; IMPA

Chemical and Physical Properties

Molecular Weight: 140

Solubility in Water: 48 g/liter (estimated; Lyman et al., 1982)

Specific Gravity: 1.109 (Rosenblatt et al., 1975)

Log Octanol/Water Partition Coefficient (K_{ow}): -0.54 (Small 1984)

1/ Compiled from: Various referenced sources.
2/ Note that both names refer to the same compound. The form encountered in the environment will be dependent on ambient pH conditions.

Soil/Water Partition Coefficient (K_{oc}): Not Applicable

Bioconcentration Factor: Not Applicable

Vapor Pressure: Not Located

Henry's Law Constant: Not Applicable

Transport and Fate

Scant data are available on the transport and fate processes for IMPA/IMP in environmental media. The form which is likely to occur in the environment (free acid or salt) will be governed by ambient pH conditions. The pKa value for IMPA is well below the normal range of pHs typical of soil or water (Small 1984). Therefore, it is likely that the predominant form will be a salt with cations such as Na^{+}, Ca^{++}, and Al^{+++} (Small 1984). The estimated vapor pressure indicates the potential for some volatilization; however, in moist soils or water the solubility of IMPA would probably tend to offset volatilization. IMPA appears to be fairly resistant to hydrolysis. In a study by Howells et al. (1973) no hydrolysis of IMPA to methylphosphonic acid (a principal hydrolysis product) was observed after several months in a hydroponic solution.

In a study by Cook et al. (1978), IMPA was utilized by selected strains of sewage bacteria as a phosphorus source. Daughton et al. (1979) found IMPA to be less bound than MPA to spodosol, a soil with high binding affinity for inorganic orthophosphate. Little sorption of IMPA to soils is expected to occur given its high water solubility. The combined low organic partitioning behavior and high water solubility suggest that IMPA will be a mobile contaminant.

Bioconcentration data for IMPA/IMP were not located in available literature. However, given the high aqueous solubility and low organic partitioning, bioconcentration would not be expected to occur.

No data on the persistence of IMPA in air, soil or water was located in available literature.

Health Effects

Mecler (1981) has evaluated the mammalian toxicity of sodium IMPA. No signs of irritation were observed following ocular administration of sodium IMPA in rabbits. Similarly, no signs of systemic toxicity were noted following application of sodium IMPA (2.0 g/kg) to intact and abraded rabbit skin; however, mild skin irritation was evident (Mecler 1981). Sodium IMPA (0.1 percent solution) did not induce dermal sensitization in guinea pigs injected intradermally over a three-week period (Mecler 1981).

In a subchronic toxicity test with sodium IMPA, rats were administered the compound in their drinking water at concentrations of 300, 1,000, or 3,000 ppm for a period of 90 days (Mecler 1981). No changes in body weight, food intake, water intake, clinical chemistry or hematological parameters were seen in treated rats compared to controls (Mecler 1981). The highest identified No-Observed-Effect-Level (NOEL) was 3,000 ppm (300 mg/kg). Sodium IMPA did not exert a mutagenic effect in any of five Salmonella strains in the Ames Assay when tested with or without liver activation (Mecler 1981). No data on reproductive toxicity, teratogenicity, chronic toxicity or carcinogenicity were located in available literature.

The oral LD_{50} values of sodium IMPA in male and female rats are 7,650 mg/kg and 6,070 mg/kg, respectively (Mecler 1981). In mice, the LD_{50} values are 5,620 and 6,550 in male and female mice, respectively (Mecler 1981).

Toxicity to Wildlife and Domestic Animals

No data on the toxicity of IMPA to wildlife or domestic animals was located in available literature.

Regulations and Standards

None located.

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

For IMPA, the D_T value is based on the results of a subchronic (90-day) toxicity study utilizing rats (Mecler 1981). In this study, rats were administered concentrations of sodium IMPA (300, 1,000, and 3,000 ppm) in drinking water. Parameters monitored in the study included body weight, food intake, water intake, clinical chemistry and hematology. No effects on any of these parameters were observed at any treatment level and therefore the highest No-Observed-Effect-Level (NOEL) identified from the study was 3,000 ppm (300 mg/kg/day). An Uncertainty Factor of 1,000 is included in the derivation of the D_T to address the extrapolation of results to humans (10), intraspecies variability (sensitive subgroups) (10) and to account for the use of a subchronic rather than a chronic exposure duration (10). Derivation of the D_T for IMPA is as follows:

$$D_T = \frac{\text{NOEL}}{\text{UF}} \text{ (mg/kg/day)}$$

$$= \frac{300}{1{,}000}$$

$$= 0.30 \text{ mg/kg/day}$$

REFERENCES

ASTM. 1985. Standard Practice for conducting bioconcentration tests with fishes and saltwater bivalve mollusca. Designation E 1022-84, pages 590-62. In: 1985 Annual Book of ASTM Standards Volume 11.04. American Society for Testing and Materials, Philadelphia, Pennsylvania.

COOK, A.M., C.G. DAUGHTON, and M. ALEXANDER. 1978. Phosphonate utilization by bacteria. J. Bacteriol. 133:85-90

DAUGHTON, C.G., A.M. COOK and M. ALEXANDER. 1979. Phosphate and soil binding: Factors limiting bacterial degradation of ionic phosphorus-containing pesticide metabolites. Applied Environmental Microbiology. 37:605-609.

DAVIES, R.P. and A.J. DOBBS. 1984. The prediction of bioconcentration in fish. Water Res. 18(10):1253-1262.

HOWELLS, D.J., J.L. HAMBROOK, D. UTLEY, AND J. WOODAGE. 1973. Degradation of phosphonates. II. The influence of the O-Alkyl group on the breakdown of some O-Alkyl methylphosphonofluoridates in wheat plants. Pesticide Science. 4:239-245.

KADEG, R.D., PAVLOU, S.P., DUXBURY, A.S. 1986. Elaboration of Sediment Normalization Theory for Non-Polar Hydrophobic Organic Chemicals. U.S. Environmental Protection Agency, Criteria and Standards Division, Washington D.C.

LYMAN, W.J., LORETI, C.P. 1986. Prediction of Soil and Sediment Sorption for Organic Compounds (Comment Final Draft). U.S. Environmental Protection Agency, Monitoring and Data Support Division, Office of Water Regulations and Standards. Washington D.C.

LYMAN, W.J., W.F. REEHL AND D.H. ROSENBLATT. 1982. Handbook of Chemical Property Estimation Methods: Environmental Behavior of Organic Compounds. McGraw-Hill Book Co., New York, NY.

MECLER, F.J. 1981. Mammalian Toxicological Evaluation of DIMP and DCPD (Phase III-IMPA). Final Report. Litton Bionetics, Inc., Kensington, MD. Prepared for: U.S. Army Medical Research and Development Command, Fort Detrick, Frederick, MD. Contract No. DAMD 17-77-C-7003.

ROSENBLATT, D.H., T.A. MILLER, J.C. DACRE, I. MUUL and D.R. COGLEY. 1975. Problem definition studies on potential environmental pollutants. II. Physical, chemical, toxicological, and biological properties of 16 substances. Technical Report 7509. U.S. Army Medical Bioengineering Research and Development Laboratory, Fort Detrick, Frederick, MD.

SMALL, M.J. 1984. Compounds Formed From the Chemical Decontamination of HD, GB, and VX and Their Environmental Fate. Technical Report 8304. United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL). Fort Detrick, Frederick, MD. NTIS No. AD-A149515.

LEAD[1/]

Summary

Lead is a heavy metal that exists in one of three oxidation states, 0, +2, and +4. There is suggestive evidence that some lead salts are carcinogenic, inducing kidney tumors in mice and rats. Lead is also a reproductive hazard, and it can adversely affect the brain and central nervous system by causing encephalopathy and peripheral neuropathy. Chronic exposure to low levels of lead can cause subtle learning disabilities in children. Exposure to lead can also cause kidney damage and anemia and may have adverse effects on the immune system.

CAS Number: 7439-92-1

Chemical Formula: Pb

IUPAC Name: Lead

Chemical and Physical Properties

Atomic Weight: 207.19

Boiling Point: 1,740°C

Melting Point: 327.5°C

1/ Compiled from: U.S. Environmental Protection Agency, Office of Waste Program Enforcement. September 1985. Chemical, physical, and biological properties of compounds present at hazardous waste sites. A Final Report Prepared by Clement Associates, Inc., Arlington, Virginia.

Also: United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL). 1985. Physical, Chemical, and Toxicological Data Summaries of 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

Specific Gravity: 11.35 at 20°C (liquid)

Vapor Pressure: 1.77 mm Hg at 1,000°C (Merck, 1983)

Solubility in Water: Insoluble; some organic compounds are soluble

Solubility in Organics: Soluble in HNO_3 and hot, concentrated H_2SO_4

Transport and Fate

Some industrially produced lead compounds are readily soluble in water (USEPA 1979). However, metallic lead and the common lead minerals are insoluble in water. Natural compounds of lead are not usually mobile in normal surface or groundwater because the lead leached from ores is absorbed by ferric hydroxide or combines with carbonate or sulfate ions to form insoluble compounds.

Movement of lead and its inorganic and organolead compounds as particulates in the atmosphere is a major environmental transport process. Lead carried in the atmosphere can be removed by either wet or dry deposition. Although little evidence is available concerning the photolysis of lead compounds in natural waters, photolysis in the atmosphere occurs readily. These atmospheric processes are important in determining the form of lead entering aquatic and terrestrial systems.

The transport of lead in the aquatic environment is influenced by the speciation of the ion. Lead exists mainly as the divalent cation in most unpolluted waters and becomes adsorbed into particulate phases. However, in polluted waters organic complexation is most important. Volatilization of lead compounds probably is not important in most aquatic environments.

Sorption processes appear to exert a dominant effect on the distribution of lead in the environment. Adsorption to inorganic solids, organic materials, and hydrous iron and manganese oxides

usually controls the mobility of lead and results in a strong partitioning of lead to soils and the bed sediments in aquatic systems. The sorption mechanism most important in a particular system varies with geological setting, pH, Eh, availability of ligands, dissolved and particulate ion concentrations, salinity, and chemical composition. The equilibrium solubility of lead with carbonate, sulfate, and sulfide is low. Over most of the normal pH range, lead carbonate, and lead sulfate control solubility of lead in aerobic conditions, and lead sulfide and the metal control solubility in anerobic conditions.

Lead in soil is not easily taken up by plants, and therefore its availability to terrestrial organisms is somewhat limited. Biomethylation of lead by microorganisms can remobilize lead to the environment. Bioaccumulation of lead has been demonstrated for a variety of organisms. Bioconcentration factors in freshwater organisms range from 42 to 1,700 for four invertebrate and two fish species (USEPA 1986). In saltwater organisms, available bioconcentration factors range from 17 to 2,600 (USEPA 1986). Microcosm studies indicate that lead is not biomagnified through the food chain.

Health Effects

There is evidence that several lead salts are carcinogenic in mice or rats, causing tumors of the kidneys following oral or parenteral administration. Data concerning the carcinogenicity of lead in humans are inconclusive. The available data are not sufficient to evaluate the carcinogenicity of organic lead compounds or metallic lead. Lead has been classified according to EPA's Guidelines for Carcinogenic Risk Assessment in EPA's Group B2 (sufficient evidence in animals) based upon the evidence of kidney tumors in rats following oral administration and inadequate evidence in humans (50 Federal Register 46971, Wed. Nov. 13, 1985).

There is equivocal evidence that exposure to lead causes genotoxicity in humans and animals. The available evidence indicates that lead presents a hazard to reproduction and exerts a toxic effect on conception, pregnancy, and the fetus in humans and experimental animals (USEPA 1977, 1980).

Many lead compounds are sufficiently soluble in body fluids to be toxic (USEPA 1977, 1980). Exposure of humans or experimental animals to lead can result in toxic effects in the brain and central nervous system, the peripheral nervous system, the kidneys, and the hematopoetic system. The metabolism and retention of lead (primarily in bone) has been well studied. Chronic exposure to inorganic lead by ingestion or inhalation can cause lead encephalopathy, and severe cases can result in permanent brain damage. Lead poisoning may cause peripheral neuropathy both in adults and children. Permanent learning disabilities in children that are clinically undetectable maybe caused by exposure to relatively low levels of lead. Short-term exposure to lead can cause reversible kidney damage however, prolonged exposure at high concentrations may result in progressive kidney damage and kidney failure. Anemia, due to inhibition of hemoglobin synthesis and a reduction in the life span of circulating red blood cells, is an early manifestation of lead poisoning. Several studies with experimental animals suggest that lead may interfere with various aspects of the immune response.

Young children are deemed a high risk group for lead exposure for a number of reasons: 1) their dietary intake in mg/kg body weight is higher than that of adults; 2) young children tend to ingest greater quantities of dirt than do adults (and such soil, particularly in urban areas, can be highly contaminated) and 3) some young children have a pica habit and may consume old, lead-based paint peelings.

Toxicity to Wildlife and Domestic Animals

Freshwater vertebrates and invertebrates are more sensitive to lead in soft water than in hard water (USEPA 1980, 1983). At a hardness of about 50 mg/liter $CaCO_3$, the median effect concentrations for nine

families range from 140 µg/liter to 236,000 µg/liter. Chronic values for Daphnia magna and the rainbow trout are 12.26 and 83.08 µg/liter, respectively, at a hardness of about 50 mg/liter. Acute-chronic ratios calculated for three freshwater species ranged from 18 to 62. Freshwater algae show an inhibition of growth at concentrations above 500 µg/liter.

Acute values for twelve saltwater species range from 476 µg/liter for the common mussel to up to 27,000 µg/liter for the soft shell clam. The acute-chronic ratio for this species is 118. Reported bioconcentration factors range from 17.5 for the Quahog clam to 2,570 for the blue mussel. Saltwater algae are adversely affected at lead concentrations as low as 15.8 µg/liter.

Lead is known to occur in the tissue of many free-living wild animals, including birds, mammals, fishes, and invertebrates. Reports of avian poisoning usually involve waterfowl ingesting spent lead shot with grit pebbles which they swallow to aid in digestion. Typical signs of avian lead poisoning include regurgitation, tremors, wing-droop, slowness and reluctance to move and anorexia (Hudson et al., 1984). There is some evidence that lead, at concentrations occasionally found near roadsides and smelters, can eliminate or reduce populations of bacteria and fungi on leaf surfaces and in soil. Many of these microorganisms play key roles in the decomposer food chain.

Cases of lead poisoning have been reported for a variety of domestic animals, including cattle, horses, dogs, and cats. Several types of anthropogenic sources are cited as the source of lead in these reports. Because of their indiscriminate eating habits, cattle often experience the greatest incidence of lead toxicity among domestic animals.

Regulations and Standards

Ambient Water Quality Criteria (USEPA 1986):

The concentrations below are for active lead, which is defined as the lead that passes through a 0.45-μm membrane filter after the sample is acidified to pH 4 with nitric acid.

Aquatic Life (Freshwater)

Acute toxicity: $e^{(1.34\ [\ln(\text{hardness})] - 2.014)}$ μg/liter
Chronic toxicity: $e^{(1.34\ [\ln(\text{hardness})] - 5.245)}$ μg/liter

At hardness of 50,100 and 200 mg/l $CaCO_3$ the acute criteria are 34, 82, and 200 μg/l.

At hardness of 50,100 and 200 mg/l $CaCO_3$ the chronic criteria are 1.3, 3.2, and 7.7 μg/l.

Aquatic Life (Saltwater)

Acute toxicity: 140 μg/liter
Chronic toxicity: 5.6 μg/liter

Human Health

Criterion: 50 μg/liter

National Primary Drinking Water Standard (USEPA): 20 μg/liter
(Proposed RMCL; 50 Federal Register 46971 Wednesday, November 13, 1985)

NIOSH Recommended Standard: TWA[1/] = 0.10 mg/m^3 (inorganic lead)

OSHA Standard: TWA = 50 μg/m^3

1/ Time Weighted Average

ACGIH Threshold Limit Values:

TWA = 0.15 mg/m^3 (inorganic dusts and fumes)
STEL[1/] = 0.45 mg/m^3 (inorganic dusts and fumes)

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

For lead, the the D_T value is based on blood lead levels at which no observed adverse effects to human health are apparent based on children as the sensitive subgroup. Typically, the health effects of lead in both humans and animals are measured by relating blood lead (PbB) levels to various adverse effects. Several studies suggest that there may be no threshold for certain lead-induced effects; however, it is not considered appropriate with the present state of understanding to conclude that blood lead levels of zero must be achieved to avoid adverse effects (USEPA 1985). In developing the RMCL for lead, EPA determined that effects seen at blood lead levels between 15 and 20 µg/dl do not constitute biologically significant adverse effects in their own right; although they may be preclinical indicators of adverse effects which could develop with increased exposure (USEPA 1985).

For protection of the more sensitive members of the population (i.e., pregnant women and their fetuses and young children), EPA advises that the blood lead level should be limited to between 15 and 20 µg/dl, as some researchers (Harris and Holley 1972; Hubermont et al. 1978) have indicated that the ratio of fetal/maternal blood lead is close to 1:1. Therefore, a No-Observed-Adverse-Effect-Level (NOAEL) for both children and adults is 15 µg/dl (blood lead).

1/ Short Term Effect Level

The D_T value for lead is calculated in the same manner as the Recommended Maximum Contaminant Level (RMCL) (50 Federal Register 46971 Wednesday, November 13, 1985) and the lifetime health advisory level for lead (USEPA 1985). Blood lead levels protective of children are converted to daily intake rates (µg/day) by using the proportionality-constant derived from the data of Ryu et al. (1983). From these data, a proportionality-constant applicable to children (blood lead = 0.16x dietary lead; units: (µg/dL)(µg/day)), who absorb a greater amount of ingested lead is used; however, a proportionality-constant reflecting the intake rate of adults is also available. An Uncertainty Factor (UF) of 5 is employed to account for intra-human variability. Because the end-points measured are extremely subtle and sensitive, EPA feels that a full order-of-magnitude UF is not required. D_T is converted to units of mg/kg/day by utilizing the weight of a reference child (10 kg) and a conversion factor (µg to mg). Derivation of this D_T value is as follows:

$$D_T = \frac{\text{NOAEL (µg/dL blood)}}{\text{Proportionality Constant x UF}}$$

$$= \frac{15\ \mu g/dL}{(0.16)(5)}$$

$$= \frac{18.75\ \mu g/day}{\text{reference weight}}$$

$$= \frac{18.75\ \mu g/day}{10\ kg}$$

[Note: EPA rounds 18.75µg to 20µg in their derivations.]

$$= 1.88 \times 10^{-3}\ mg/kg/day$$

REFERENCES

AMERICAN CONFERENCE OF GOVERNMENTAL INDUSTRIAL HYGIENISTS (ACGIH). 1980. Documentation of the Threshold Limit Values. 4th ed. Cincinnati, Ohio. 488 pages.

DOULL, J. KLASSEN, L.D., AND AMDUR, M.O., eds. 1980. Casarett and Doull's Toxicology: The Basic Science of Poisons. 2nd ed. Macmillan Publishing Co., New York. 778 pages.

HARRIS, P. AND M.R. HOLLEY. 1972. Lead levels in cord blood. Pediatrics. 49:606-608.

HUBERMONT, G., J.P. BUCHET, H. ROELS AND R. LAUWERYS. 1978. Placental transfer of lead, mercury, and cadmium in women living in a rural area: Importance of drinking water in lead exposure. Int. Occup. Environ. Health. 41:117-124.

HUDSON, R.H., TUCKER, R.K. AND HAEGALE, M.A. 1984. Handbook of Toxicity of Pesticides to Wildlife. Second Edition. United States Department of the Interior Fish and Wildlife Service. Resource Publication 153. Washington, D.C. 1984.

INTERNATIONAL AGENCY FOR RESEARCH ON CANCER (IARC). 1980. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. Vol. 23: Some Metals and Metallic Compounds. World Health Organization, Lyon, France. Pp. 325-415.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH). 1983. Registry of Toxic Effects of Chemical Substances. Data Base. Washington, D.C. October 1983.

NRIAGU, J.O., ed. 1978. The Biogeochemistry of Lead in the Environment. Part B. Biological Effects. Elsevier/North-Holland Biomedical Press, New York. 397 pages.

RYU, J.E., E.E. ZIEGLER, F.E. NELSON and S.J. FOMON. 1983. Dietary intake of lead and blood lead concentration in early infancy. Am. J. Dis. Child. 137:886-891.

THE MERCK INDEX. 1983. An Encyclopedia of Chemicals, Drugs and Biologicals. Tenth Edition. Merck and Co., Inc. Rahway, New Jersey.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1977. Air Quality Criteria for Lead. Office of Research and Development, Washington, D.C. December 1977. EPA 600/8-77-017.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1979. Water-Related Environmental Fate of 129 Priority Pollutants. Washington, D.C. December 1979. EPA 440/4-79-029.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1980. Ambient Water Quality Criteria for Lead. Office of Water Regulations and Standards, Criteria and Standards Division, Washington, D.C. October 1980. EPA 440/5-80-057.

U.S ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1983. Draft Revised Section B of Ambient Water Quality Criteria for Lead. Office of Water Regulations and Standards, Criteria and Standards Division, Washington, D.C. August 1983.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1984. Health Effects Assessment for Lead. Final Draft. Environmental Criteria and Assessment Office, Cincinnati, Ohio. September 1984. ECAO-CIN-H055.

U.S. Environmental Protection Agency (USEPA). 1985. Draft Health Advisory for Lead. Office of Drinking Water. U.S. Environmental Protection AGency, Washington, D.C. September 30, 1984.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1986. Quality Criteria for Water, 1986 ("The Gold Book"). Office of Water Regulations and Standards, Washington, DC. EPA 440/5-86-001.

WEAST, R.E., ed. 1981. Handbook of Chemistry and Physics. 62nd ed. CRC Press, Cleveland, Ohio. 2,332 pages.

WORLD HEALTH ORGANIZATION. 1977. Environmental Health Criteria: 3. Lead. World Health Organization, Geneva. 160 pages.

LEWISITE/LEWISITE OXIDE[1/]

Summary

Lewisite is an arsenic-containing compound formerly manufactured as a chemical warfare agent. Lewisite oxide is the hydrolysis product of Lewisite. Both are vesicants (blister agents) and highly toxic. The acute oral LD_{50} in rats for Lewisite oxide is 5 mg/kg. In humans, inhalation of 6 ppm Lewisite for 30 minutes is lethal. There is evidence linking lewisite exposure and the development of certain cancers in humans.

CAS Numbers: 541-25-3 (Lewisite)
333-25-5 (Lewisite oxide)

Chemical Formula: $C_2H_2AsCl_3$ (Lewisite)
C_2H_2AsClO (Lewisite oxide)

IUPAC Name: Dichloro-(2-chlorovinyl)arsine (Lewisite)
Dichloro-(2-chlorovinyl)arsine oxide (Lewisite oxide)

Important Synonyms and Trade Names: Lewisite; Lewisite oxide

Chemical and Physical Properties[2/]

Molecular Weights: 207 (Lewisite) (Merck 1983)
153 (Lewisite oxide) (USAMBRDL 1985)

Melting Point: 0.1°C (Merck 1983)

1/ Compiled from: United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL). 1985. Physical, Chemical, and Toxicological Data Summaries of 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

2/ For Lewisite unless otherwise specified.

Boiling Point: ~ 190°C (Merck 1983)

Specific Gravity: 1.88 (Merck 1983)

Solubility in Water: Insoluble [Lewisite] (Merck 1983)

Solubility in Organics: Soluble in most organic solvents (Merck 1983)

Vapor Pressure: 0.395 mm Hg at 20°C (Merck 1983)
0.58 mm Hg at 25°C (DA 1974)

Vapor Density: 7.1 (USEPA 1985)

Transport and Fate

Very little data is available on the fate or transport of Lewisite and Lewisite oxide in environmental media. In aqueous solution, Lewisite or the oxide is easily oxidized to 2-chlorovinyl-arsonic acid by a variety of oxidants (Rosenblatt et al. 1975). Lewisite is also rapidly hydrolyzed to Lewisite oxide. The latter may further combine with water to form a geminal diol which is slightly acidic. No information is available on the transport of Lewisite/Lewisite oxide via volatilization; however, the vapor pressure of Lewisite indicates the potential for some volatility. Interactions of Lewisite with airborne water vapors could result in hydrolysis to Lewisite oxide.

In soil, it is thought that Lewisite behaves in a manner analogous to sodium arsenite, and is oxidized presumably by microorganisms (Rosenblatt et al. 1975). Oxidation of Lewisite or its oxide to the less toxic form--2-chlorovinyl-arsonic acid is slow (Rosenblatt et al., 1975). No data on the uptake of either compound in plants or aquatic biota was located in available literature. However, because of its extreme phytotoxicity it would appear that the potential for bioconcentration of Lewisite oxide through the food chain is not likely (Rosenblatt et al., 1975).

Health Effects

Lewisite is a potent vesicant and is highly toxic by all routes of exposure. The low lethal dose in humans is 6 ppm via inhalation for a 30 minute exposure. As little as 2 ml of Lewisite via dermal exposure can be fatal (Merck 1983). Eye lesions can be incurred at concentrations of 20 mg/m^3 (DA 1974). Signs and symptoms of exposure include pulmonary edema, diarrhea, restlessness, weakness, subnormal temperature and low blood pressure. Occular contact results in an immediate searing sensation with permanent loss of sight if decontamination is not immediate. Dermal contact results in stinging sensations and reddening, usually within 30 minutes. Blistering follows and usually occurs within 12 hours of contact (USEPA 1985).

No data on the chronic toxicity, reproductive toxicity, teratogenicity, or mutagenicity of Lewisite/Lewisite Oxide was located. Nishimoto et al. (1986), Shigenobu (1980), and Yamada (1963) report that retired workers formerly involved in the production of poison gases (Mustard, Lewisite and others) have a high risk of various types of malignant tumors, including cancers of the respiratory tract. However, problems associated with multiple chemical exposures of these workers precludes definative statements of the carcinogenic potential of lewisite. Krause and Grussendorf (1979) and Krause and Grussendorf (1978) report cases of Bowen's Disease, development of intraepidermal carcinoma, in two people following a past dermal exposure to Lewisite. In both cases a tumor relapse occurred following an initial surgical removal of the cancerous tissue.

In rats, the acute dermal and subcutaneous LD_{50} values for Lewisite are 24 and 1 mg/kg, respectively (NIOSH 1983); the inhalation LC_{50} for mice is 150 mg/m^3 (10 minute exposure). The oral LD_{50} for Lewisite oxide in rats is 5 mg/kg (NIOSH 1983). Dermal and subcutaneous LD_{50} values for Lewisite in guinea pigs are 12 and 1 mg/kg, respectively (NIOSH 1983). In rabbits, the oral and intravenous LD_{50} values for Lewisite oxide are 3 and 1 mg/kg. The oral and subcutaneous LD_{50} values for Lewisite oxide in the guinea pig are 2 and 0.2 mg/kg (NIOSH 1983).

Toxicity to Wildlife and Domestic Animals

Little data is available on the toxicity of Lewisite/Lewisite oxide to wild or domestic animals. The dermal and subcutaneous LD_{50} values for Lewisite in dogs are 15 and 2 mg/kg, respectively (NIOSH 1983). In rabbits, the dermal, subcutaneous and intravenous LD_{50} values for Lewisite are 6, 2 and 0.5 mg/kg, respectively (NIOSH 1983).

Regulations and Standards

OSHA Threshold Limit Values (NIOSH 1983): TWA[1/] = 0.5 mg/m^3 (as As for Lewisite)

TWA = 0.5 mg/m^3 (as As for Lewisite oxide)

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

For Lewisite/Lewisite oxide, the D_T value is derived from an acute oral toxicity value (LD_{50}) for Lewisite oxide in guinea pigs. The D_T is computed as the product of the acute value and an application factor of 1×10^{-5} (Layton et al., 1986). The application factor allows the derivation of an interim acceptable long-term intake rate (D_T) based on the results of acute tests (LD_{50}) in the absence of more suitable long-term studies (i.e., No-Observed-Effect-Level, NOEL, studies). The application factor corresponds to the cumulative percentile on a lognormal distribution of NOEL/LD_{50} ratios for various chemicals. The percentile was chosen to reduce the probability that the

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1/ Time Weighted Average

calculated dose rate would be above a toxic level; the 5th cumulative percentile was used by Layton et al. (1986) and was found to be equal to 10^{-3}. The application factor also includes a safety factor of 100 to address interspecies and intraspecies variability; therefore, an interim estimate of D_T is obtained when the application factor is multiplied by the acute value. Derivation of this D_T value is as follows:

$$D_T = \text{Acute oral } LD_{50} \times \text{Application Factor}$$
$$= 2 \text{ mg/kg/day} \times 1 \times 10^{-5}$$
$$= 0.00002 \text{ mg/kg/day}$$

REFERENCES

DEPARTMENT OF THE ARMY (DA). 1974. Chemical Data Sheets. Volume I. Lewisite. Edgewood Arsenal Special Report. Aberdeen Proving Ground, MD. Report Number EO-SR-74001. December 1974.

KRAUSE, H. and E.I. GRUSSENDORF. 1979. Therapy of Morbus Bowen with 5-Fluorouracil Ointment (English Translation). Derm. Beruf Umwelt. 27(6):176-178 [English Abstract from CancerLit, a computerized database.]

KRAUSE, H. and E.I. GRUSSENDORF. 1978. A Causal Relation Between Bowen's Disease and a Lewisite Scar (English Translation). Hantarzt. 29(9):490-493 [English Abstract From CancerLit, a computerized database.]

LAYTON, D.W., MALLOU, B.J., ROSENBLATT, D.H. and SMALL, M.J. 1986. Deriving Allowable Daily Intakes For Systemic Toxicants Lacking Chronic Toxicity Data. Regulatory Toxicology and Pharmacology. In Press.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH). 1983. Registry of Toxic Effects of Chemical Substances (RTECS). Volume I-III. U.S. Department of Health and Human Services. Cincinnati, OH.

NISHIMOTO, Y., M. YAMAKIDO, T. SHIGENOBU, M. YUKUTAKE, and S. MATSUSAKA. 1986. Cancer of the Respiratory Tract Observed in Workers Having Retired From a Poison Gas Factory (English Translation). Gan To Kagaku Ryoho. 13(4 part 2):1144-1148 [English Abstract from CancerLit, a computerized database.]

ROSENBLATT, D.H., T.A. MILLER, J.C. DACRE, I. MUUL and D.R. COGLEY. 1975. Problem definition studies on potential environmental pollutants. II. Physical, chemical, toxicological, and biological properties of 16 substances. Technical Report 7509. U.S. Army Medical Bioengineering Research and Development Laboratory, Fort Detrick, Frederick, MD.

SHIGENOBU, T. 1980. Occupational Cancer of the Lungs: Cancer of the Respiratory Tract Among Workers Manufacturing Poisonous Gases. Nippon Kyobu Shikkan Gakkai Zasshi. 18(12):880-885 [English Abstract from CancerLit, a computerized database.]

THE MERCK INDEX. 1983. An Encyclopedia of Chemicals, Drugs and Biologicals. Tenth ed. Windholz, M., Budavan, S., Blumetti, R.F. and Otterbein, E.S. (eds.). Merck and Company, Inc., Rahway, New Jersey.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1985. Chemical Emergency Preparedness Program. Interim Guidance. Chemical Profiles. Office of Solid Waste and Emergency Response, USEPA, Washington, D.C. Revision No. 1. 9223.0-1A.

UNITED STATES ARMY MEDICAL BIOENGINEERING RESEARCH AND DEVELOPMENT LABORATORY (USAMBRDL), 1985. Physical, Chemical, and Toxicological Data Summaries for 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

YAMADA, A. 1963. On the Late Injuries Following Occupational Inhalation of Mustard Gas, with Special References to Carcinoma of the Respiratory Tract. Acta Pathol. Jpn. 13(3):131-155.

MALATHION[1/]

Malathion is a member of the organophosphorous class of pesticides. Its primary mode of toxicity (acute and chronic exposures) is via the inhibition of the enzyme acetycholinesterase in peripheral and central nervous systems. Chronic exposure to high levels of malathion in rats resulted in reduced food intake and weight gain. Effects on reproductive parameters were observed in rats fed diets containing 4,000 ppm malathion. Both positive and negative results have been obtained in mutagenicity tests utilizing bacterial and mammalian test systems. No evidence of carcinogenicity has been observed in several studies utilizing rats and mice.

CAS Number: 121-75-5

Chemical Formula: $C_{10}H_{19}PO_6S_2$

IUPAC Name: S-(1,2-dicarbethoxyethyl)O,O-dimethyldithiophosphate

Important Synonyms and Trade Names: Malathion

Chemical and Physical Properties

Molecular Weight: 330 (Merck 1983)

Boiling Point: 156°C at 0.7 mm Hg (Merck 1983)

Melting Point: 2.9°C (Merck 1983)

1/ Compiled from: United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL), 1985. Physical, Chemical, and Toxicological Data Summaries for 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

Also: National Academy of Science (NAS). 1977. Drinking Water and Health. Volume I. National Academy of Sciences, Washington, DC. pg. 620-626.

Solubility in Water: 145 mg/liter (Merck 1983)

Solubility in Organics: Miscible with numerous organic solvents

Log Octanol/Water Partition Coefficient (K_{ow}): 2.89 (Freed et al. 1979)

Soil/Water Partition Coefficient (K_{oc}):

283	Lyman et al. (1982) Eqn 4-5 (S = 145)
901	Lyman et al. (1982) Eqn 4-8 (log K_{ow} = 2.9)
524	Lyman and Loreti (1986) Eqn I (log K_{ow} = 2.9)
520	Lyman and Loreti (1986) Eqn II (log K_{ow} = 2.9)
522	Lyman and Loreti (1986) Eqn III (log K_{ow} = 2.9)
761	Kadeg et al. (1986) (log K_{ow} = 2.9)

Bioconcentration Factor:

37.3	Davies and Dobbs (1984) Eqn A (S = 145)
92.6	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 2.89)
49	Davies and Dobbs (1984) Eqn C (log K_{ow} = 2.89)
82	Davies and Dobbs (1984) Eqn B (log K_{ow} = 2.89)

Vapor Pressure: 4×10^{-5} mm Hg at 30°C (Merck 1983)
2.4×10^{-5} mm Hg at 25°C (Lyman et al. 1982) Estimated

Henry's Law Constant: 7.2×10^{-8} atm-m^3/mole (Calculated)
9×10^{-8} atm-m^3/mole (calculated)

Transport and Fate

The somewhat low vapor pressure indicates that volatilization is not a major transport process for malathion from environmental media, however, it may be enhanced by covaporization with water. The stability of malathion in aqueous solution is pH dependent (NAS 1977). At a pH of 9, the halflife of malathion is 12 hours; it is hydrolyzed instantly at a more alkaline pH of 12. At more acidic pH values of 5-7, essentially no hydrolysis occurs (NAS 1977). The half-life of malathion in raw river water is reported to be less than one week; in distilled water it is

stable up to three weeks (NAS 1977). It is thought that the differences in residence time are a function of biological activity. The National Academy of Science (1977) summarize data in which malathion introduced into collected water samples at concentrations of 10 mg/liter was degraded almost completely after ten days. In general, malathion is degraded in water more rapidly than other organophosphorous compounds under similar conditions (NAS 1977).

A range of estimated soil/water partition coefficients (K_{oc}) is reported above and indicates that sorption of malathion to soils/sediments and dissolved organic material will occur. Pavlou (1980) estimates that sorption of organophosphorous insecticides will range from low to moderate. The combined water solubility and organic partitioning of malathion suggest that this compound will exhibit some degree of environmental mobility.

A range of estimated bioconcentration factors (BCFs) for malathion is also reported above. ASTM (1985) indicates that chemicals with bioconcentration factors less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the concentration factors suggests that appreciable bioconcentration or biomagnification of malathion residues is not likely to occur.

Health Effects

The primary health effect stemming from exposure to organophosphorous compounds like malathion, is through inhibition of the enzyme acetylcholinesterase. Inhibition is increased as a result of the oxidative conversion of malathion to malaoxon *in vivo*, a more potent inhibitor of acetylcholinesterase (Casarett and Doull 1980). In humans, severe exposure to organophosphates can result in respiratory failure due to paralysis of the respiratory muscles, bronchoconstriction and bronchial secretion, and depression of the respiratory center in the brain (Casarett and Doull 1986).

Chronic feeding studies (2 years) with malathion at dosages of 100, 1,000, and 5,000 ppm resulted in no gross effects in rats at the 100 and 1,000 ppm dosages (NAS 1977; cite Hazleton and Holland 1953). At 5,000 ppm, food intake and weight gain were reduced. Significant decreases in plasma, erythrocyte and brain cholinesterase activity occurred in the two high dose groups. In another chronic feeding study dosages of 500, 5,000, and 20,000 ppm in the diet of rats resulted in significant inhibition of erythrocyte cholinesterase activity at all dosages. Reduced growth and food intake were observed in the highest dose group (NAS 1977; cite Golz and Shaffer 1956). Subacute toxicity studies with dosages ranging from 100 to 5,000 ppm also revealed no effect on food intake, weight gain or growth, but significant decreases in cholinesterase activity were observed at the higher dosages.

Reproductive effects have been observed in rats fed diets containing 4,000 ppm malathion. The number of newborn rats alive at one week was 105 for controls and 56 for treated animals. Only 34 treated animals survived to weaning at age 21 days, compared with 75 controls. Average body weights of treatment animals were significantly lower than control body weights (NAS 1977 cite Kalow and Marton 1961).

Malathion has yielded positive results for mutagenicity in tests with numerous bacterial and mammalian test systems including: E. Coli K12; Salmonella (activated); Chinese hamster fibroblasts; Chinese hamster V79 cells; mouse primary spermatocyte and rat bone marrow cells (NIOSH 1983). Significant (positive) results were also obtained following a mutagenicity test with human fetal lung fibroblasts (NIOSH 1983). No evidence of carcinogenicity has been observed in several studies with mice and rats.

The low oral lethal dose of malathion in humans ranges between 246 and 857 mg/kg. The acute oral LD_{50} in rats and mice are 370 and 770 mg/kg, respectively (NIOSH 1983).

Toxicity to Wildlife and Domestic Animals

Salmonids and centrarchids appear to be the freshwater fish most sensitive to malathion. Many aquatic invertebrates appear to be more sensitive than fish to malathion (USEPA 1986a). The 96-hour LC_{50} ranges between 101 and 285 µg/liter for three centrarchid and three salmonid species (USEPA 1986a). The 96-hour LC_{50} for the rainbow trout (Salmo gairdneri) is 68 µg/liter and 50 µg/liter in the largemouth bass (Micropterus salmoides). The 96-hour LC_{50} for the invertebrate Gammarus lacustris is reported to be 1.0 µg/liter.

The acute oral LD_{50} values of malathion in mallard ducks, pheasants and songbirds are 1,485 mg/kg, 167 mg/kg and 403 mg/kg, respectively (Hudson et al., 1984). The range in values illustrates the species sensitivity. The acute intraperitoneal LD_{50} in dogs is 1,857 mg/kg and 550 mg/kg in guinea pigs. The acute oral and dermal LD_{50} values for rabbits are 250-1,200 and 4,100, respectively, and in guinea pigs, 570 and 6,700 mg/kg, respectively (USAMBRDL 1985).

Regulations and Standards

Ambient Water Quality Criteria (USEPA 1986a):

Aquatic Life (Freshwater):

Acute Toxicity: Data are inadequate
Chronic Toxicity: 0.01 µg/liter

Aquatic Life (Saltwater):

Acute Toxicity: Data are inadequate
Chronic Toxicity: 0.01 µg/liter

Human Health:

No criterion has been established.

ACGIH Threshold Limit Value (NIOSH 1983): TWA[1/] = 10 mg/m^3 (skin)

OSHA Threshold Limit Value: TWA = 15 mg/m^3 (skin)

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

For malathion, the D_T value is based on the same data used by EPA to compute the current Risk Reference Dose (RfD) (USEPA 1986b). The RfD is based on a subchronic oral toxicity study in human volunteers (male) (Rider et al. 1959). The groups of subjects were administered malathion in capsule doses of 8 mg/day for 32 days, 16 mg/day for 47 days or 24 mg/day for 56 days. Cholinesterase activity was determined before and after administration of the chemical. The toxicological endpoint of interest was decreased erythrocyte and plasma cholinesterase activity. The No-Observed-Effect Level (NOEL) identified from this study was 16 mg/day (0.23 mg/kg/day assuming a 70 kg reference human weight). An Uncertainty Factor (UF) of 10 was employed to address intraspecies variability (sensitive subgroups) (10). [Note: a factor of 10 was not included by EPA to address the use of a subchronic study because the critical toxic effect--cholinesterase inhibition--is thought to be independent of exposure duration.] Derivation of the D_T value for malathion is as follows:

1/ Time Weighted Average

$$D_T = \frac{\text{NOEL mg/kg/day}}{\text{UF}}$$

$$= \frac{0.23}{10}$$

$$= 0.023 \text{ mg/kg/day}$$

References

ASTM. 1985. Standard Practice for conducting bioconcentration tests with fishes and saltwater bivalve mollusca. Designation E 1022-84, pages 590-62. In: 1985 Annual Book of ASTM Standards Volume 11.04. American Society for Testing and Materials, Philadelphia, Pennsylvania.

CASARETT and DOULL'S TOXICOLOGY. 1980. The Basic Science of Poisons. Second Edition. Doull, J., Klaassen, C.D., and Amdur, M.O. (Editors). Macmillan Publishing Company, Inc., New York. 778 pp.

CASARETT and DOULL'S TOXICOLOGY. 1986. The Basic Science of Poisons. Third Edition. Doull, J., Klaassen, C.D., and Amdur, M.O. (Editors). Macmillan Publishing Company, Inc., New York.

DAVIES, R.P. and A.J. DOBBS. 1984. The prediction of bioconcentration in fish. Water Res. 18(10):1253-1262.

HUDSON, R.H., TUCKER, R.K. AND HAEGALE, M.A. 1984. Handbook of Toxicity of Pesticides to Wildlife. Second Edition. United States Department of the Interior Fish and Wildlife Service. Resource Publication 153. Washington, D.C. 1984.

KADEG, R.D., PAVLOU, S.P., DUXBURY, A.S. 1986. Elaboration of Sediment Normalization Theory for Non Polar Hydrophobic Organic Chemicals. U.S. Environmental Protection Agency, Criteria and Standards Division, Washington D.C.

KALOW, W. and MARTON, A. 1961. Second generation toxicity of malathion in rats. Nature. 192:464-465.

LYMAN, W.J., LORETI, C.P. 1986. Prediction of Soil and Sediment Sorption for Organic Compounds (Comment Final Draft). U.S. Environmental Protection Agency, Monitoring and Data Support Division, Office of Water Regulations and Standards. Washington D.C.

LYMAN, W.J., W.F. REEHL AND D.H. ROSENBLATT. 1982. Handbook of Chemical Property Estimation Methods: Environmental Behavior of Organic Compounds. McGraw-Hill Book Co., New York, NY.

NATIONAL ACADEMY OF SCIENCE (NAS). 1977. Drinking Water and Health. Volume I. National Academy of Sciences, Washington, DC. pg. 797.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH). 1983. Registry of Toxic Effects of Chemical Substances. Volumes I-III. Department of Health and Human Services. Cincinnati, OH.

PAVLOU, S.P. 1980. Thermodynamic Aspects of Equilibrium Sorption of Persistent Organic Molecules at the Sediment-Seawater Interface: A Framework For Predicting Distributions in the Aquatic Environment. IN: Contaminants and Sediments. Volume 2. Baker, R.A. (Editor). Science Publishers, Inc. Ann Arbor, MI.

RIDER, J.A., H.C. MOELLER, J. SWADER, AND R.G. DEVEREAUX. 1959. A study of the anticholinesterase properties of EPN and malathion in human volunteers. Clinical Research. 1:81.

THE MERCK INDEX. 1983. An Encyclopedia of Chemicals, Drugs and Biologicals. Tenth ed. Windholz, M., Budavan, S., Blumetti, R.F. and Otterbein, E.S. (eds.). Merck and Company, Inc., Rahway, New Jersey.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1986a. Quality Criteria for Water, 1986 ("The Gold Book"). Office of Water Regulations and Standards, Washington, DC. EPA 440/5-86-001.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1986b. Risk Reference Dose for Malathion. Integrated Risk Information System (IRIS). [Note: This is an EPA computerized database.]

UNITED STATES ARMY MEDICAL BIOENGINEERING RESEARCH AND DEVELOPMENT LABORATORY (USAMBRDL). 1985. Physical, Chemical, and Toxicological Data Summaries of 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

MERCURY (INORGANIC)[1/]

Summary

Inorganic mercury is reported to be teratogenic and embryotoxic in studies with experimental animals. In humans, prenatal exposure to mercury vapors has been associated with spontaneous abortions and infant mortalities. The major target organs for inorganic mercury compounds are the central nervous system and the kidneys. Mutagenic responses in mammalian cell cultures have been equivocal.

CAS Number: 7439-97-6

Chemical Formula: Hg

IUPAC Name: Mercury

Chemical and Physical Properties

Atomic Weight: 200.59 (Merck 1983)

Boiling Point: 356.72°C (Merck 1983)

Melting Point: -38.87°C (Merck 1983)

Specific Gravity: 13.534 (Merck 1983)

1/ Compiled from: U.S. Environmental Protection Agency, Office of Waste Program Enforcement. September 1985. Chemical, physical, and biological properties of compounds present at hazardous waste sites. A Final Report Prepared by Clement Associates, Inc., Arlington, Virginia.

Also: U.S. Environmental Protection Agency (USEPA). 1984. Mercury Health Effects Update. Health Issue Assessment. Final Report. Office of Health and Environmental Assessment. Washington, D.C. EPA-600/8-84-019F.

Solubility in Water: 56.2 µg/liter at 25°C (Merck 1983)

Solubility in Organics: Depends on chemical species

Vapor Pressure: 0.0012 mm Hg at 20°C (USEPA 1984a)
0.002 mm/Hg at 25°C (Merck 1983)

Transport and Fate

Inorganic mercury can exist in three oxidative states in the environment, including metallic (Hg°), mercurous (Hg_2^{++}) and mercuric (Hg^{++}). In general, the mercurous salts are much less soluble than the more commonly found mercuric salts. The nature and solubility of the chemical species that occur in an environmental system will depend on the redox potential and the pH of the environment.

Mercury can volatilize to the atmosphere from aquatic and terrestrial sources. Volatilization is reduced by conversion of metallic mercury to complexed species and by deposition of HgS in reducing sediments, but even so, atmospheric transport is a major environmental distribution pathway for mercury (USEPA 1984a). Precipitation (wet/dry) is an important mechanism for removal of mercury from the atmosphere (USEPA 1984a). Photolysis is important in the breakdown of airborne mercurials and may be important in some aquatic systems.

Adsorption onto suspended and bed sediments is probably the most important process determining the fate of mercury in the aquatic environment. Sorption is strongest into organic material for the Hg (+2) species. Mercury in soils is generally complexed to organic compounds. Mercury is not readily leached from either organic rich or mineral rich soils (Rosenblatt et al., 1975). Uptake of mercury in plants can occur with the highest concentrations generally found in bulb or root crops (Rosenblatt et al., 1975). Turf grass exposed to a mixture of mercurous and mercuric chloride added to the root zone did not accumulate mercury (USEPA 1984a). Uptake of mercury vapor by wheat leaves has been observed (USEPA 1984a).

Virtually any mercury compound can be remobilized in aquatic systems by microbial conversion to methyl and dimethyl forms. Conditions reported to enhance biomethylation include large amounts of available mercury, large numbers of bacteria, the absence of strong complexing agents, near neutral pH, high temperatures, and moderately aerobic environments.

Inorganic mercury is bioaccumulated by numerous organisms (USEPA 1984b). In freshwater, bioconcentration factors for mercury in mercuric chloride range from 1,800 in rainbow trout (Salmo Gairdneri) to 4,994 in the fathead minnow (Pimephales promelas) (USEPA 1984b). ASTM (1985) indicates that chemicals with bioconcentration factors less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the reported concentration factors suggests that appreciable bioconcentration or biomagnification of mercury can occur.

Health Effects

Occupational studies indicate that the chronic exposure to mercury vapor (Hg°) affects primarily the central nervous system and the kidneys (increased urinary excretion of high molecular weight proteins) (USEPA 1984a). Acute exposure to high vapor concentrations can cause erethism (behavioral effects), metal fume fever, pneumonitis, bronchitis, chest pains, dyspnea, coughing, stomatitis, gingivitis, salivation, and diarrhea (USEPA 1984a). In case reports, acute mercury vapor exposures have been shown to cause exudative alveolar and intestinal edema and erosion and desquamation and necrosis of the bronchiolar epithelium (USEPA 1984a). Contact dermatitis may result from exposure to liquid metallic mercury (USEPA 1984a). Soluble mercuric salts are highly toxic following ingestion as compared with the less soluble mercurous compounds.

In early studies, women chronically exposed to mercury vapor experienced increased frequencies of menstrual disturbances and spontaneous abortions (USEPA 1984a). Rats exposed to mercury vapors

(2.5 mg/m^3, 6 hr/day, 5 day/week) exhibited longer estrus cycles (USEPA 1984a). Inorganic mercuric mercury (Hg^{++}) is translocated across the blood-brain and placental barriers to a lesser degree than Hg°, and therefore inorganic salts are less likely to affect the central nervous system and the fetus (USEPA 1984a). Infants 4 to 30 months appear to be more susceptible than adults and older children to the effects of mercury vapors (USEPA 1984a). Placental transport of mercury and subsequent oxidation in fetal tissues has been demonstrated in mice (USEPA 1984a). However, no conclusive results concerning the teratogenic effects of mercury vapor are available (USEPA 1984a). Parenteral administration of inorganic mercury salts has produced abnormalities in experimental animals (USEPA 1984a). Gale (1981) reported a number of abnormalities in hamster fetuses given a subcutaneous dose of mercury acetate on day eight of gestation, including pericardial cavity distension, cleft palate, hydrocephalus and heart defects (USEPA 1984a).

Mutagenic responses have been equivocal following exposure of non-mammalian cell cultures to mercuric salts in vitro (USEPA 1984a). Chromosomal aberrations have been observed in lymphocytes of persons occupationally exposed to mercury vapors (USEPA 1984a). Carcinogenesis in humans has not been associated with occupational exposure to mercury vapors (USEPA 1984a). Mercury has been classified according to EPA's Guidelines for Carcinogenic Risk Assessment in EPA's Group D (not classified) based upon inadequate data in animals and humans (50 Federal Register 46972, Wed. Nov. 13, 1985).

Toxicity to Wildlife and Domestic Animals

The aquatic toxicity of inorganic mercury compounds has been investigated. Among freshwater species, the 96-hour LC_{50} values for inorganic mercuric salts range from 0.02 µg/liter for crayfish to 2,000 µg/liter for caddisfly larvae (USEPA 1980). Mercuric chloride is acutely toxic to rainbow trout at about 300 µg/liter at 10°C (USEPA 1984a).

The acute oral lethal dose (low) in rabbits is 40 mg/kg (NIOSH 1983). Chronic dietary exposure of chickens to mercuric chloride at growth inhibitory levels causes immune suppression with a differential reduction effect on specific immunoglobulins (Bridger and Thaxton 1983). The lethal concentration (LC_{50}) values for mercuric chloride administered in the diets of Japanese quail (Coturnix c. japonica), ringed-neck pheasants (Phasianus colchicus) and mallard ducks (Anas platyrhynchos) were 5,926, 3,790, and >5,000 ppm, respectively (Hill et al., 1975).

Regulations and Standards

Ambient Water Quality Criteria (USEPA 1986a):

Aquatic Life (Freshwater)

Acute toxicity: 2.4 µg/liter
Chronic toxicity: 0.012 µg/liter

Aquatic Life (Saltwater)

Acute toxicity: 2.1 µg/liter
Chronic toxicity: 0.025 µg/liter

Human Health

Criterion: 144 ng/liter

National Primary Drinking Water Standard (USEPA): 0.003 mg/liter (Proposed RMCL; 50 Federal Register 46972 Wednesday, November 13, 1985).

NIOSH Recommended Standard: TWA[1/] inorganic mercury = 0.05 mg/m^3

OSHA Standard (skin): Ceiling Level = 0.1 mg/m^3

ACGIH Threshold Limit Values:

TWA (vapor) = 0.05 mg/m^3

TWA (aryl and inorganic compounds) = 0.1 mg/m^3

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

For inorganic mercury the D_T value for oral exposure is based on the same data used by EPA to compute the current Risk Reference Dose (RfD) (USEPA 1986b). The RfD is based on a chronic (2-year) oral toxicity study utilizing rats (male and female) fed dietary concentrations of 0.5, 2.5, 10, 40, or 160 ppm mercury as mercury acetate in the diet (Fitzhugh et al. 1950). Assuming a food consumption rate equal to 5 percent bw/day, the daily intake is 0.025, 0.125, 0.5, 2.0 and 8.0 mg/kg (USEPA 1986b). Detailed histological evaluations of a number of tissues were performed. The kidney was the only tissue affected with lesions occurring in the proximal convoluted tubules and cortex. Lesions were not present at doses below 2.0 mg/kg/day. Though the 0.025, 0.125, and 0.5 mg/kg/day doses appear to have been No-Observed-Adverse-Effect-Levels (NOAELs), EPA has instead based the RfD on the Lowest-Observed-Adverse-Effect-Level (LOAEL) of 2.0 mg/kg/day. This was done because the descriptive manner in which the data from the Fitzhugh et al. study are presented make it difficult to evaluate the histopathological findings for these doses (USEPA 1986b). In light of this uncertainty, the 2.0 mg/kg/day LOAEL was chosen by EPA as the basis for an RfD calculation.

An Uncertainty Factor (UF) of 1,000 is included in the derivation of the RfD to account for extrapolation of the data to humans (10), intraspecies variability (sensitive subgroups) (10) and to address the use of a LOAEL rather than a NOAEL (10). Derivation of the oral D_T value for inorganic mercury is as follows:

$$D_T = \frac{LOAEL}{UF} \text{ (mg/kg/day)}$$

$$= \frac{2.0}{1000}$$

$$= 0.002 \text{ mg/kg/day}$$

An inhalation D_T has also been developed for inorganic mercury because of its potential for volatilization. The inhalation D_T is based on the same approach used by EPA to compute the Acceptable Intake Chronic for inhalation exposure (USEPA 1984c). The intake value is derived from a Threshold Limit Value (TLV) for mercury vapor of 0.05 mg/m^3 (ACGIH 1983). In using this value as a basis for an acceptable intake, EPA has first added an extra margin of safety to the TLV by incorporating an UF of 10. The TLV is thus reduced to 0.005 mg/m^3. The acceptable intake chronic is then computed by using an estimated breathing rate (BR--20 m^3/day) and multiplying by 5/7 days to correct for continuous exposure. An additional UF of 10 is included by EPA to protect sensitive subgroups and a 70 kg reference weight is included for adult humans. Derivation of the D_T for inhalation exposure to inorganic mercury vapor is as follows:

$$D_T = \frac{TLV/UF \times BR \times 5/7 \text{ days}}{70 \text{ kg} \times UF}$$

$$= \frac{0.005 \text{ mg/m}^3 \times 20 \text{ m}^3\text{/day} \times 5/7 \text{ days}}{70 \text{ kg} \times UF}$$

$$= 0.000102 \text{ mg/kg/day}$$

REFERENCES

ASTM. 1985. Standard Practice for conducting bioconcentration tests with fishes and saltwater bivalve mollusca. Designation E 1022-84, pages 590-62. In: 1985 Annual Book of ASTM Standards Volume 11.04. American Society for Testing and Materials, Philadelphia, Pennsylvania.

1/ Time Weighted Average.

AMERICAN CONFERENCE OF GOVERNMENTAL INDUSTRIAL HYGIENISTS (ACGIH). 1980. Documentation of the Threshold Limit Values. 4th ed. Cincinnati, Ohio. 488 pages.

AMERICAN CONFERENCE OF GOVERNMENTAL INDUSTRIAL HYGIENISTS (ACGIH). 1983. Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom Environment with Intended Changes for 1984. Cincinnati, OH.

BRIDGER, M.A., and THAXTON, J.P. 1983. Humoral immunity in the chicken as affected by mercury. Arch. Environ. Contam. Toxicol. 12:45-49.

HILL, E.F., HEATH, R.G., SPANN, J.W., WILLIAMS, J.D. 1975. Lethal Dietary Toxicities of Environmental Pollutants to Birds. U.S. Department of Interior Fish and Wildlife Service Special Scientific Report. Wildlife No. 191.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH). 1983. Registry of Toxic Effects of Chemical Substances. Data Base. Washington, D.C. October 1983.

ROSENBLATT, D.H., T.A. MILLER, J.C. DACRE, I. MUUL AND D.R. COGLEY. 1975. Problem definition studies on potential environmental pollutants. II. Physical, chemical, toxicological, and biological properties of 16 substances. Technical Report 7509. U.S. Army Medical Bioengineering Research and Development Laboratory, Fort Detrick, Frederick, MD.

SHEPARD, T.H. 1980. Catalog of Teratogenic Agents. 3rd ed. Johns Hopkins University Press, Baltimore. 410 pages.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1979. Water-Related Environmental Fate of 129 Priority Pollutants. Washington D.C. December 1979. EPA 440/4-79-029.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1980. Ambient Water Quality Criteria for Mercury. Office of Water Regulations and Standards, Criteria and Standards Division. Washington, D.C. October 1980. EPA-440/5-80-058.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1984a. Mercury Health Effects Update. Health Issue Assessment. Final Report. Office of Health and Environmental Assessment. Washington, D.C. EPA-600/8-84-019F.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1984b. Ambient Water Quality Criteria for Mercury. Office of Water Regulations and Standards, Criteria and Standards Division. Washington, D.C. EPA 440/5-84-026. January 1985.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1984c. Health Effects Assessment for Mercury. Environmental Criteria and Assessment Office, Cincinnati, Ohio. September 1984. ECAO-CIN-H042 (Final Draft).

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1984. Water Quality Criteria; Request For Comments. Federal Register 49:4551-4553.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1986a. Quality Criteria for Water, 1986 ("The Gold Book"). Office of Water Regulations and Standards, Washington, DC. EPA 440/5-86-001.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1986b. Risk Reference Dose for Inorganic Mercury. Integrated Risk Information System (IRIS). [Note: This is an EPA computerized data base].

WEAST, R.E., ed. 1981. Handbook of Chemistry and Physics. 62nd ed. CRC Press, Cleveland, Ohio. 2,332 pages.

WORLD HEALTH ORGANIZATION (WHO). 1976. Environmental Health Criteria: 1. Mercury. World Health Organization, Geneva. 131 pages.

METHYLARSONIC ACID[1/]

Summary

No data on the carcinogenicity of methylarsonic acid (MAA) or its sodium salts were located in available literature. Rabbits subchronically dosed with the monosodium salt of MAA at a level of 50 mg/kg in the diet exhibited toxic hepatitis. MAA and its mono- and disodium salts were not mutagenic in tests with Salmonella, E. coli, B. subtilis or S. cerevisiae.

CAS Number: 124-58-3 (acid)
2163-80-6 (monosodium salt)
144-21-8 (disodium salt)

Chemical Formulae: $CH_3AsO(OH)_2$ (acid)
$CH_3AsO(OH)ONa$ (monosodium salt)
$CH_3AsO(ONa)_2$ (disodium salt)

IUPAC Name: Methylarsonic acid
Monosodium methanearsonate
Disodium monomethanearsonate

Important Synonyms and Trade Names: Methanearsonic acid;
Monosodium methylarsonate;
Disodium methanearsonate.

Chemical and Physical Properties

Molecular Weight: 139.9 (acid)
161.9 (monosodium salt)
183.9 (disodium salt)

Melting Point: 115-119°C [monosodium salt] (IARC 1980)
132-139°C [disodium salt] (IARC 1980)
161°C [acid] (Merck 1983)

Solubility in Water: 254 g/liter at 25°C [acid] (ISHOW 1983)
570 g/liter at 25°C [monosodium salt] (IARC 1980)
300 g/liter at 25°C [disodium salt] (IARC 1980)

Solubility in Organics: Soluble in methanol; insoluble in other organic solvents

Log Octanol/Water Partition Coefficient (K_{ow}): Not Located

Soil/Water Partition Coefficient (K_{oc}): Not Applicable

Bioconcentration Factor: Not Applicable

Vapor Pressure: Not Located

Henry's Law Constant: Not Applicable

Transport and Fate

No data on the vapor pressure of MAA were located. However, a portion of MAA may be reduced to volatile arsines under both aerobic and anaerobic conditions. Braman (1975) detected the volatile alkylarsines dimethyl arsine and trimethylarsine above grass which had been treated with MAA and other organoarsenicals. Volatile arsenicals (dimethylarsine) were detected following treatment of soils with the monosodium salt of methanearsonic acid (MSMA), sodium arsenate and cacodylic acid (Woolson 1976). In this study, the amounts volatilized under aerobic conditions during a 150-day period were 8.22, 0.64, and 14.1 percent, respectively. Under anaerobic conditions, the amount of MSMA volatilized was reduced to 0.84 percent (Woolson 1976).

Microbial degradation of MAA does occur. In soil samples taken from field plots treated with MAA, degradation products were dimethylarsenic acid (cacodylic acid) and arsenate (Woolson 1982). It was thought that MAA may also form insoluble compounds which are not immediately subject to degradation as indicated by the detection of

significant amounts of MAA over 1 year post-application (Woolson 1982). Demthylation of monosodium MAA also occurs (NAS 1977). In a loam soil, 1.7 - 10 percent was degraded to [C^{14}] carbon dioxide and arsenates (more toxic). A fungus and two actinomycetes isolated from this soil degraded 3, 13, and 9 percent of added monosodium MAA (NAS 1977).

Organoarsenicals such as MAA are absorbed by clay soils (IARC 1980). Sorption processes involve the arsenic moieties of organoarsenical compounds and it is this portion which likely controls the movement of these compounds in soils (Wauchope 1976). Sorption is typically governed by the prevailing aluminum and ferrous oxide content of the ambient soil. Both the amount and rate of leaching of MAA and its sodium salts are increased when soil is coarse and the aluminum and iron contents are low (NAS 1977). Quantitative partitioning data for MAA were not located in available literature.

Data specific for the bioaccumulative potential of MAA or its sodium salts were not located. However, a similar organoarsenical compound, dimethyl arsenic acid (DMAA), has been shown to bioaccumulate in exposed (10.6 µg/l) algae and daphnids (Isensee et al. 1973). In this study, fish and snails did not bioaccumulate DMAA, indicating little transfer between food chain organisms.

Health Effects

No data were located on the toxicity of MAA in humans. Exon et al. (1974) administered the monosodium salt of MAA in the diets of adult male and female rabbits for up to 52 weeks. Toxic hepatitis coincided with daily oral doses of 1.5 mg As/kg bw following 7 and 12 weeks of exposure. Vacuolization of the livers of treated animals was also observed. Following 12 weeks of exposure to the contaminated diet, all females were bred and a pair of offspring from each mating were killed at 1 and 20 days of age to determine the possibility of arsenic contamination occurring *in uteri* or from exposed nursing females. Analyses of arsenic residues in these offspring indicated that arsenic transfer did not occur.

MAA and both the mono- and disodium salts gave negative results in the Salmonella microsome test, in DNA repair tests in E. coli and B. subtilis and in an assay for mitotic recombination in Saccharomyces cerevisiae (IARC 1980). The monosodium salt of MAA was not mutagenic in the Salmonella spot test (No metabolic activation)(IARC 1980). No data on the carcinogenicity of MAA or its mono- or disodium salts were located in available literature.

Acute data are available for the sodium salts of MAA. The acute LD_{50} for technical MAA (disodium salts) in rats by oral administration is about 2,800 mg/kg, and 700 mg/kg for the monosodium salt (NIOSH 1983). The intraperitoneal LD_{50} for the disodium salt of MAA is 600 and 681 mg/kg in male and female mice respectively, and 600 and 561 mg/kg in male and female rats, respectively (IARC 1980).

Toxicity to Wildlife and Domestic Animals

No data on the toxicity of MAA or its sodium salts to mammalian or avian wildlife were located in available literature. Acute 96-hour LC_{50} values are available for the monosodium salt of methylarsonic acid (MSMA). All values listed below are representative of static test conditions and for mature organisms. Data are from Mayer and Ellersieck (1986):

Species	Chemical Description	96-hour LC_{50} (mg/l)
Gammarus Fasciatus	34.8 percent liquid concentrate	>100
Rainbow Trout	51.2 percent liquid concentrate	78.0
Goldfish	34.8 percent liquid concentrate	31.1
Fathead Minnow	34.8 percent liquid concentrate	13.3
Channel Catfish	37.7 percent spray concentrate	26.8
Bluegill	34.8 percent liquid concentrate	12.0
Bluegill	37.7 percent spray concentrate	49.2
Bluegill	51.2 percent liquid concentrate	>100

Regulations and Standards

OSHA TWA[1/]: 0.5 mg/m^3 [as arsenic]
ACGIH Threshold Limit Value: TWA = 0.2 mg/m^3 [as arsenic]

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

A long term feeding study (up to 52 weeks) in rabbits was available for the monosodium salt of MAA. However, this study was not considered appropriate for development of a D_T value as only one dose level was tested (50 ppm MAA, monosodium salt) (Exon et al. 1974). In the study, groups of rabbits were necropsied at various intervals up to 52 weeks and histological findings reported. Toxic hepatitis was observed in rabbits necropsied at 7 and 12 weeks exposure but not in other animals. Exon et al. (1974) also report the presence of liver vacuolization in all other treated rabbits. A reduction in the rations of contaminated feed to rabbits after 10 weeks (but not the chemical concentration) resulted in a disappearance of the toxic hepatitis. These findings indicate that dietary administration of 50 ppm MAA monosodium salt to rabbits resulted in significant effects; therefore, these data are not used as a basis for the MAA D_T value.

For methylarsonic acid (monosodium salt), the D_T value is derived from an acute oral toxicity value (LD_{50}) in rats. The D_T is computed as the product of the acute value and an application factor of 1×10^{-5} (Layton et al., 1986). The application factor allows the derivation of an interim acceptable longterm intake rate (D_T) based on the results of acute tests (LD_{50}) in the absence of more suitable

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1/ Time Weighted Average

longterm studies (i.e., No-Observed-Effect-Level, NOEL, studies). The application factor corresponds to the cumulative percentile on a lognormal distribution of NOEL/LD_{50} ratios for various chemicals. The percentile was chosen to reduce the probability that the calculated dose rate would be above a toxic level; the 5th cumulative percentile was used by Layton et al. (1986) and was found to be equal to 10^{-3}. The application factor also includes a safety factor of 100 to address interspecies and intraspecies variability; therefore, an interim estimate of D_T is obtained when the application factor is multiplied by the acute value. Derivation of this D_T value is as follows:

$$D_T = \text{Acute oral } LD_{50} \times \text{Application Factor}$$
$$= 700 \text{ mg/kg/day} \times 1 \times 10^{-5}$$
$$= 0.007 \text{ mg/kg/day}$$

REFERENCES

AMERICAN CONFERENCE OF GOVERNMENTAL INDUSTRIAL HYGIENISTS (ACGIH). 1980. Documentation of Threshold Limit Values for Substances in Workroom Air. Cincinnati, OH.

BRAMAN, R.S. 1975. Arsenic in the environment. In: A. Woolson (ed.) Arsenical Pesticides. American Chemical Society (ACS) Symposium Series 7. American Chemical Society. Washington, D.C. pp. 108-123.

EXON, J.H., J.R. HARR, and R.R. CLAEYS. 1974. The effects of long term feeding of monosodium acid methanearsonate (MSMA) to rabbits. Nutrition Reports International. 9(5):351-357.

IARC (International Agency for Research on Cancer). 1980. IARC Monographs on The Evaluation of the Carcinogenic Risk of Chemicals to Humans. Volume 23: Some Metals and Metallic Compounds. IARC, Switzerland.

ISENSEE, A.R., P.C. KEARNEY, E.A. WOOLSON, G.E. JONES and V.P. WILLIAMS. 1973. Distribution of alkyl arsenicals in a model ecosystem. Environ. Sci. Technol. 7(9):841-845.

LAYTON, D.W., MALLOU, B.J., ROSENBLATT, D.H. and SMALL, M.J. 1986. Deriving Allowable Daily Intakes For Systemic Toxicants Lacking Chronic Toxicity Data. Regulatory Toxicology and Pharmacology. In Press.

MAYER, F.L. and M.R. ELLERSIECK. 1986. Manual of Acute Toxicity: Interpretation and Data Base for 410 Chemicals and 66 Species of Freshwater Animals. United States Department of the Interior. Fish and Wildlife Service. Washington, D.C. Resource Publication No. 160.

NATIONAL ACADEMY OF SCIENCES (NAS 1977). Medical and Biologic Effects of Environmental Pollutants. Arsenic. Committee on Medical and Biologic Effects of Environmental Pollutants. National Academy of Sciences. Washington, D.C. 332 pp.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH). 1983. Registry of Toxic Effects of Chemical Substances. Volumes I-III. Department of Health and Human Services. Cincinnati, OH.

THE MERCK INDEX. 1983. An Encyclopedia of Chemicals, Drugs and Biologicals. Tenth Edition. Rathway, New Jersey, Merck and Company, Inc.

WAUCHOPE, D. 1976. Acid dissociation constants of arsenic acid, methylarsonic acid (MAA), dimethylarsinic acid (cacodylic acid) and N-(phosphonomethyl)glycine. J. Agric. Food Chem. 24(4):717-721.

WOOLSON, E.A. 1976. Generation of dimethyl arsine from soil. Presented at the Sixteenth Annual Meeting of the Weed Science Society of America. Paper No. 218. (Cited in NAS 1977, above).

WOOLSON, E.A., N. AHARONSON AND R. IADEVAIA. 1982. Application of the high-performance liquid chromatography-flameless atomic absorption method to the study of alkyl arsenical herbicide metabolism in soil. J. Agric. Food Chem. 30(3):580-584.

METHYLENE CHLORIDE[1/]

Summary

Methylene chloride (dichloromethane) increased the incidence of lung and liver tumors and sarcomas in exposed rats and mice. Methylene chloride yielded positive results in mutagenicity tests utilizing bacterial test systems. In humans, methylene chloride irritates the eyes, mucous membranes, and skin. Exposure to high levels adversely affects the central and peripheral nervous systems and the heart. In experimental animals, methylene chloride is reported to cause kidney and liver damage, convulsions, and paresis (incomplete paralysis).

CAS Number: 75-09-2

Chemical Formula: CH_2Cl_2

IUPAC Name: Dichloromethane

Important Synonyms and Trade Names: Methylene dichloride, methane dichloride

Chemical and Physical Properties

Molecular Weight: 84.93

1/ Compiled from: U.S. Environmental Protection Agency, Office of Waste Program Enforcement. September 1985. Chemical, physical, and biological properties of compounds present at hazardous waste sites. A Final Report Prepared by Clement Associates, Inc., Arlington, Virginia.

Also: United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL). 1985. Physical, Chemical, and Toxicological Data Summaries of 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

Boiling Point: 40°C (USEPA, 1979)

Melting Point: -95.1°C

Specific Gravity: 1.3266 at 20°C

Solubility in Water: 13,200-20,000 mg/liter at 25°C (USEPA, 1979)
19,000 mg/liter (Valvani et al., 1980)

Solubility in Organics: Miscible with alcohol and ether

Log Octanol/Water Partition Coefficient: 1.25 (USEPA, 1979)
2.90 (USEPA, 1985a)

Soil/Water Partition Coefficient (K_{oc}):

27.5	Sabljic (1984) (experimental)
20.6	Lyman et al. (1982) Eqn 4-5 (S = 17,000)
114	Lyman et al. (1982) Eqn 4-8 (log K_{ow} = 1.25)
27	Lyman and Loreti (1986) Eqn I (log K_{ow} = 1.25)
22	Lyman and Loreti (1986) Eqn II (log K_{ow} = 1.25)
23	Lyman and Loreti (1986) Eqn III (log K_{ow} = 1.25)
50	Kadeg et al. (1986) (log K_{ow} = 1.25)
257	Lyman et al. (1982) Eqn 4-8 (log K_{ow} = 1.9)
87; 76; 78	Lyman and Loreti (1986) Eqn I, II, III (log K_{ow} = 1.9)
146	Kadeg et al. (1986) (log K_{ow} = 1.9)

Bioconcentration Factor:

2.9 - 2.3	Davies and Dobbs (1984) Eqn A (S = 13,200 - 20,000)
5.25	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 1.25)
8.60	Davies and Dobbs (1984) Eqn C (log K_{ow} = 1.25)
5.81	Davies and Dobbs (1984) Eqn B (log K_{ow} = 1.25)
16.4	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 1.9)
21	Davies and Dobbs (1984) Eqn B (log K_{ow} = 1.9)
14.2	Davies and Dobbs (1984) Eqn C (log K_{ow}) = 1.9)

Vapor Pressure: 362 mm Hg at 20°C (USEPA 1985a)
436 mm Hg at 25°C (Berkowitz et al., 1978)

Vapor Density: 2.93

Henry's Law Constant: 2.6×10^{-3} atm-m^3/mole (Calculated)
2.03×10^{-3} atm-m^3/mole (USEPA 1985a)

Transport and Fate

Volatilization to the atmosphere appears to be the major mechanism for removal of methylene chloride from aquatic systems and its primary environmental transport process (USEPA 1979). Photooxidation in the troposphere appears to be the dominant chemical fate of methylene chloride following its release to the air. Once in the troposphere, the compound is attacked by hydroxyl radicals, resulting in the formation of carbon dioxide, and to a lesser extent, carbon monoxide and phosgene. Phosgene is readily hydrolyzed to HCl and CO_2. About one percent of tropospheric methylene chloride would be expected to reach the stratosphere where it would probably undergo photodissociation resulting from interaction with high energy ultraviolet radiation. Aerial transport of methylene chloride is partly responsible for its relatively wide environmental distribution. Atmospheric methylene chloride may be returned to the earth in precipitation.

Photolysis, oxidation, and hydrolysis do not appear to be significant environmental fate processes for methylene chloride. A range of experimental and estimated soil-water partition coefficients (K_{oc}) is reported above and indicates that some sorption of methylene chloride to soils/sediments and dissolved organic material will occur. Pavlou (1980) estimates that sorption of volatile organic compounds will range from low to moderate. The combined high water solubility and low organic partitioning of methylene chloride suggest that this compound will exhibit a high degree of environmental mobility. Although methylene chloride is potentially biodegradable, especially by acclimatized microorganisms, biodegradation occurs at a very slow rate.

A range of bioconcentration factors (BCFs) for methylene chloride is also reported above. ASTM (1985) indicates that chemicals with bioconcentration factors (BCF) less than approximately 100 have low potential for causing harm to wildlife and human health via

biomagnification of residues up food chains. The magnitude of the concentration factors suggest that appreciable bioconcentration or biomagnification of methylene chloride residues is not likely to occur.

Health Effects

Methylene chloride is currently under review by the National Toxicology Program (NTP 1984, USEPA 1985). Preliminary results indicate that it produced an increased incidence of lung and liver tumors in mice and mammary tumors in female and male rats. In a chronic inhalation study, male rats exhibited an increased incidence of sarcomas in the ventral neck region (Burek et al. 1984); however, the authors suggest that the relevance and toxicological significance of this finding is uncertain in light of available toxicity data. Methylene chloride has been classified according to EPA's Guidelines for Carcinogenic Risk Assessment, in EPA's Group B2 (probable human carcinogen), based upon positive results in animal studies and inadequate evidence in humans (USEPA 1985b).

Methylene chloride is reported to be mutagenic in bacterial test systems. It has also produced positive results in the Fischer rat embryo cell transformation test. However, it has been suggested that the observed cell-transforming capability may have been due to impurities in the test material. There is no conclusive evidence that methylene chloride exposure produces teratogenic effects.

In humans, direct contact with methylene chloride produces eye, respiratory tract, and skin irritation (USEPA 1985). Mild poisonings due to inhalation exposure produce somnolence, lassitude, numbness and tingling of the limbs, anorexia, and lightheadedness, followed by rapid and complete recovery. More severe poisonings generally involve correspondingly greater disturbances of the central and peripheral nervous systems. Methylene chloride also has acute toxic effects on the heart, including the induction of arrhythmia. Fatalities reportedly due to methylene chloride exposure have been attributed to cardiac injury and heart failure. Methylene chloride is metabolized to

carbon monoxide in vivo, and levels of carboxyhemoglobin in the blood are elevated following acute exposures. In experimental animals, methylene chloride is reported to cause kidney and liver damage, convulsions, and distal paresis. An oral LD_{50} value of 2,136 mg/kg, and an inhalation LC_{50} value of 88,000 mg/m^3/30 min are reported for the rat.

Toxicity to Wildlife and Domestic Animals

Very little information concerning the toxicity of methylene chloride to domestic animals and wildlife exists (USEPA 1980). Acute values for the freshwater species Daphnia magna, the fathead minnow, and bluegill are 224,000, 193,000, and 224, 000 µg/liter, respectively. Acute values for the saltwater mysid shrimp and sheepshead minnow, are 256,000 and 331,000 µg/liter, respectively. No data concerning chronic toxicity are available. The 96-hour EC_{50} values for both freshwater and saltwater algae are greater than the highest test concentration, 662,000 µg/liter.

Regulations and Standards

Ambient Water Quality Criteria (USEPA 1986):

Available data are not adequate for establishing criteria, however, EPA does report the lowest values known to be toxic in aquatic organisms:

Aquatic Life (Freshwater)

Acute toxicity: 11,000 µg/liter
Chronic toxicity: No data are available

Aquatic Life (Saltwater)

Acute toxicity: 12,000 µg/liter
Chronic toxicity: 6,400 µg/liter

Human Health

Due to the carcinogenicity of methylene chloride the ambient water criterion is set at zero. However, estimates of the carcinogenic risks associated with lifetime exposure from ingestion of contaminated water and contaminated aquatic organisms are:

Risk	Concentration
10^{-5}	1.9 µg/liter
10^{-6}	0.19 µg/liter
10^{-7}	0.019 µg/liter

CAG Potency Slope for Inhalation Exposure (USEPA 1985b): 1.4×10^{-2} $(mg/kg/day)^{-1}$

CAG Potency Slope for Oral Exposure (USEPA 1985b): 7.3×10^{-3} $(mg/kg/day)^{-1}$

NIOSH Recommended Standards:

TWA[1/] = 261 mg/m^3 (in the presence of no more than 9.9 mg/m^3 of CO)

Peak Concentration = 1,737 mg/m^3/15 min

OSHA Standards: TWA = 1,737 mg/m^3
Ceiling Level = 3,474 mg/m^3
Peak Concentration (5 min/3 hr) = 6,948 mg/m^3

ACGIH Threshold Limit Values: TWA = 350 mg/m^3
STEL[2/] = 1,740 mg/m^3

1/ Time Weighted Average.
2/ Short-Term Effect Level.

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

For carcinogens such as methylene chloride, the D_T value is based on the USEPA Cancer Assessment Group's cancer potency slopes. The cancer potency slopes have been estimated for oral exposure routes and for inhalation exposure for methylene chloride. The slopes are intended to be a plausible upper bound of the potency of a carcinogen in inducing cancer at low doses. Calculation of a D_T using a cancer potency slope requires selection of an acceptable cancer risk level. A range of risk levels from 10^{-4} to 10^{-7} will be considered for all carcinogens, therefore a range of D_T values is presented. Derivation of the D_T values for methylene chloride is as follows:

$$D_T = \frac{\text{Risk Level}}{\text{Potency Slope (mg/kg/day)}^{-1}}$$

$$= \frac{1 \times 10^{-4}}{1.4 \times 10^{-2} \text{ (mg/kg/day)}^{-1}}$$

$$= 7.1 \times 10^{-3} \text{ mg/kg/day}$$

The range of D_T values for methylene chloride is presented below.

Risk Level	Inhalation D_T (mg/kg/day	Oral D_T (mg/kg/day)
10^{-4}	7.1×10^{-3}	1.4×10^{-2}
10^{-5}	7.1×10^{-4}	1.4×10^{-3}
10^{-6}	7.1×10^{-5}	1.4×10^{-4}
10^{-7}	7.1×10^{-6}	1.4×10^{-5}

REFERENCES

ASTM. 1985. Standard Practice for conducting bioconcentration tests with fishes and saltwater bivalve mollusca. Designation E 1022-84, pages 590-62. In: 1985 Annual Book of ASTM Standards Volume 11.04. American Society for Testing and Materials, Philadelphia, Pennsylvania.

AMERICAN CONFERENCE OF GOVERNMENTAL INDUSTRIAL HYGIENISTS (ACGIH). 1980. Documentation of the Threshold Limit Values. 4th ed. Cincinnati, Ohio. 488 pages.

BERKOWITZ,J.G., GOYER, M.M., HARRIS, J.C., LYMAN, W.J., HORNE, R.A., NELTEN, L.H., HARRISON, J.E., and ROSENBLATT, D.H. 1978. Literature Review--Problem definition studies on selected chemicals. Final Report. Vol. II. Chemistry, toxicology, and potential environmental effects of selected organic pollutants. Contract No. DAMD 17-77-C-7037, Arthur D. Little, Inc. Cambridge, MA (AD B052946L).

BUREK, J.D., NITSCHKE, K.D., BELL, T.J., WACKERLE, D.L., CHILDS, R.C., BEYER, J.E., DITTENBER, D.A., RAMPY, L.W., AND MCKENNA, M.J. 1984. Methylene chloride: A two-year inhalation toxicity and oncogenicity study in rats and hamsters. Fundam. Appl. Toxicol. 4:30-47

DAVIES, R.P. and DOBBS, A.J. 1984. The prediction of bioconcentration in fish. Water Res. 18(10): 1253-1262.

KADEG, R.D., PAVLOU, S.P., DUXBURY, A.S. 1986. Elaboration of Sediment Normalization Theory for Non Polar Hydrophobic Organic Chemicals. U.S. Environmental Protection Agency, Criteria and Standards Division, Washington D.C.

LYMAN, W.J., REEHL, W.F., and ROSENBLATT, D.H. 1982. Handbook of Chemical Property Estimation Methods: Environmental Behavior of Organic Compounds. McGraw-Hill Book Co., New York.

LYMAN, W.J., LORETI, C.P. 1986. Prediction of Soil and Sediment Sorption for Organic Compounds (Comment Final Draft). U.S. Environmental Protection Agency, Monitoring and Data Support Division, Office of Water Regulations and Standards. Washington D.C.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH). 1976. Criteria for a Recommended Standard--Occupational Exposure to Methylene Chloride. March 1976. DHEW Publication No. (NIOSH) 76-138.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH). 1983. Registry of Toxic Effects of Chemical Substances. Data Base. Washington, D.C.

NATIONAL TOXICOLOGY PROGRAM (NTP). 1984. NTP Technical Report on the Toxicology and Carcinogenesis Studies of Methylene Chloride (CAS No. 75-09-2) in F344/N Rats and B6C3F$_1$ Mice (Inhalation Studies) NTP Technical Report No. 291. Research Triangle Park, North Carolina. USDHHS (NIH) Publication NO. 85-2562.

PAVLOU, S.P. 1980. Thermodynamic Aspects of Equilibrium Sorption of Persistent Organic Molecules at the Sediment-Seawater Interface: A Framework For Predicting Distributions in the Aquatic Environment. IN: Contaminants and Sediments. Volume 2. Baker, R.A. (Editor). Science Publishers, Inc. Ann Arbor, MI.

SAX, N.I. 1975. Dangerous Properties of Industrial Materials. 4th ed. Van Nostrand Reinhold Co., New York. 1,258 pages.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1979. Water-Related Environmental Fate of 129 Priority Pollutants. Washington D.C. December 1979. EPA 440/4-79-029.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1980. Ambient Water Quality Criteria for Halomethanes. Office of Water Regulations and Standards, Criteria and Standards Division, Washington, D.C. October 1980. EPA 440/5-80-051.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1984. Health Effects Assessment for Methylene Chloride. Environmental Criteria and Assessment Office, Cincinatti , Ohio. September 1984. ECAO-CIN-H028 (Final Draft).

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1985a. Draft Superfund Public Health Evaluation Manual. Prepared by: ICF Incorporated, Washington, D.C. USEPA. Office of Solid Waste and Emergency Response, Washington, D.C. EPA Contract No. 68-01-7090.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1985b. Health Assessment Document for Methylene Chloride. Addendum: Updated Carcinogen Assessment of Dichloromethane (Methylene Chloride). Office of Health and Environmental Assessment, Washington, D.C. September 1985. EPA 600/8-82/004FA.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1986. Quality Criteria for Water, 1986 ("The Gold Book"). Office of Water Regulations and Standards, Washington, DC. EPA 440/5-86-001.

VALVANI, S.C., YALKOWSKY, S.H., and ROSEMAN, T.J. 1980. Solubility and partitioning. IV. Aqueous solubility and octanol-water partition coefficients of liquid nonelectrolytes. J. Pharm. Sci. 70 (5):502-202.

WEAST, R.E., ed. 1981. Handbook of Chemistry and Physics. 62nd ed. CRC Press, Cleveland, Ohio. 2,332 pages.

METHYL ISOBUTYL KETONE[1/]

Summary

Methyl isobutyl ketone (MIBK) produced kidney damage in exposed rats. In humans, exposure has produced headaches, nausea, vomiting, and eye irritation. No information is available on the carcinogenicity, mutagenicity, reproductive toxicity or teratogenicity of MIBK.

CAS Number: 108-10-1

Chemical Formula: $(CH_3)_2CHCH_2COCH_3$

IUPAC Name: 4-Methyl-2-pentanone

Important Synonyms and Trade Names: Hexone, isobutyl methyl ketone, isopropyl acetone, MIBK, and MIBK

Chemical and Physical Properties

Molecular Weight: 100.2

Boiling Point: 117°C

Melting Point: -84.7°C

1/ Compiled from: U.S. Environmental Protection Agency, Office of Waste Program Enforcement. September 1985. Chemical, physical, and biological properties of compounds present at hazardous waste sites. A Final Report Prepared by Clement Associates, Inc., Arlington, Virginia.

Also: United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL). 1985. Physical, Chemical, and Toxicological Data Summaries of 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

Specific Gravity: 0.7978 at 20°C

Solubility in Water: 19,000 mg/liter (Marochini, 1984)

Solubility in Organics: Soluble in chloroform, alcohol, ether, acetone, benzene, and many other organic solvents

Log Octanol/Water Partition Coefficient (K_{ow}):

1.18

1.25 (Lyman et al., 1982) Fragment Method

Soil/Water Partition Coefficients (K_{oc}):

19	Lyman et al. (1982) Eqn 4-5 (S = 19,000)
114	Lyman et al. (1982) Eqn 4-8 (log K_{ow} = 1.25)
27	Lyman and Loreti (1986) Eqn I (log K_{ow} = 1.25)
22	Lyman and Loreti (1986) Eqn II (log K_{ow} = 1.25)
23	Lyman and Loreti (1986) Eqn III (log K_{ow} = 1.25)
50	Kadeg et al. (1986) (log K_{ow} = 1.25)

Bioconcentration Factor:

6.47	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 1.37)
2.4	Davies and Dobbs (1984) Eqn A (S = 19,000)
10.1	Davies and Dobbs (1984) Eqn B (log K_{ow} = 1.37)
5.81	Davies and Dobbs (1984) Eqn C (log K_{ow} = 1.25)
8.60	Davies and Dobbs (1984) Eqn B (log K_{ow} = 1.25)
5.25	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 1.25)

Vapor Pressure: 16 mm Hg at 20°C (TDB Peer Review Committee 1984)

20.3 mm Hg at 25°C (estimated; Lyman et al., 1982)

Henry's Law Constant: 1.1×10^{-4} atm-m^3/mole (calculated)

Vapor Density: 3.45

Flash Point: 23°C

Transport and Fate

Limited information was located on the transport and fate of methyl isobutyl ketone (MIBK) in the environment. MIBK is a volatile compound and therefore loss from environmental media due to volatilization will likely be a dominant transport process. However, because it is quite soluble in water, volatilization from water bodies or wet soil will likely be limited. In the atmosphere, MIBK may be prone to attack by hydroxy radicals (oxidation) and/or photodissociation due to interaction with strong ultraviolet radiation.

A range of estimated soil-water partition coefficients (K_{oc}) is reported above and indicates that some sorption of MIBK to soils/sediments and dissolved organic material will occur. Pavlou (1980) estimates that sorption of volatile organic compounds will range from low to moderate. The combined water solubility and low organic partitioning indicate that MIBK will be a mobile environmental contaminant. Biodegradation also may be an important fate process for MIBK in the environment.

A range of estimated bioconcentration factors (BCFs) for MIBK is also presented above. ASTM (1985) indicates that chemicals with bioconcentration factors less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the concentration factors suggests that appreciable bioconcentration or biomagnification of MIBK residues is not likely to occur.

Health Effects

No studies on the carcinogenicity, mutagenicity, reproductive toxicity or teratogenicity of methyl isobutyl ketone were found in the literature reviewed. Methyl isobutyl ketone caused headache, nausea, vomiting, and eye irritation in a number of workers exposed to concentrations of 200 to 2,000 mg/m^3. Kidney damage was observed in rats exposed to 400 mg/m^3 of MIBK for 2 weeks but the damage appeared

to be reversible. Male and female rats dosed orally with MIBK daily for 13 weeks exhibited nephrotoxicity and increased liver and kidney weights at the highest dose (1,000 mg/kg) (Microbiological Associates, Inc. 1986). These same effects were exhibited to a lesser extent in rats receiving 250 mg/kg. No effects were seen at 50 mg/kg. The acute oral LD_{50} for MIBK in rats is 2,080 mg/kg.

Toxicity to Wildlife and Domestic Animals

The only study reviewed on the toxicity of methyl isobutyl ketone to wildlife reported that the TL_{50} for brine shrimp was 1,230 mg/liter. Data on the toxicity of MIBK in terrestrial animals was not located in the literature reviewed.

Regulations and Standards

NIOSH Recommended Standards (air): TWA[1/] = 200 mg/m^3

OSHA Standards (air): TWA = 400 mg/m^3

ACGIH Threshold Limit Values: TWA = 205 mg/m^3
STEL[2/] = 300 mg/m^3

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

1/ Time Weighted Average.
2/ Short-Term Effect Level.

For MIBK, the D_T value is based on the same data used by EPA to compute the Risk Reference Dose (RfD) (USEPA 1986). The RfD is based on a subchronic oral toxicity study in which male and female rats were administered 0, 50, 250, or 1,000 mg/kg MIBK (gavage) daily (Microbiological Associates, Inc. 1986). Nephrotoxicity was generally observed for both male and female high dose rats, as were increased liver and kidney weights. However, no liver lesions were observed. The same effects were noted but to a lesser degree, in the 250 mg/kg dose group. The No-Observed-Effect-Level (NOEL) identified from this study was 50 mg/kg/day. An Uncertainty Factor of 1,000 is employed to address the extrapolation of results to humans (10), intraspecies variability (sensitive subgroups) (10) and to account for the use of a subchronic rather than a chronic experimental study (10). Derivation of the D_T value for MIBK is as follows:

$$D_T = \frac{\text{NOEL (mg/kg/day)}}{\text{UF}}$$

$$= \frac{50}{1{,}000}$$

$$= 0.05 \text{ mg/kg/day}$$

REFERENCES

AMERICAN CONFERENCE OF GOVERNMENTAL INDUSTRIAL HYGIENISTS (ACGIH). 1980. Documentation of the Threshold Limit Values. 4th ed. Cincinnati, Ohio. 488 pages.

ASTM. 1985. Standard Practice for conducting bioconcentration tests with fishes and saltwater bivalve mollusca. Designation E 1022-84, pages 590-62. In: 1985 Annual Book of ASTM Standards Volume 11.04. American Society for Testing and Materials, Philadelphia, Pennsylvania.

DAVIES, R.P. and A.J. DOBBS. 1984. The prediction of bioconcentration in fish. Water Res. 18(10):1253-1262.

KADEG, R.D., PAVLOU, S.P., DUXBURY, A.S. 1986. Elaboration of Sediment Normalization Theory for Non Polar Hydrophobic Organic Chemicals. U.S. Environmental Protection Agency, Criteria and Standards Division, Washington D.C.

LYMAN W.J., LORETI, C.P. 1986. Prediction of Soil and Sediment Sorption for Organic Compounds (Comment Final Draft). U.S. Environmental Protection Agency, Monitoring and Data Support Division, Office of Water Regulations and Standards. Washington D.C.

LYMAN, W.J., REEHL, W.F., and ROSENBLATT, D.H. 1982. Handbook of Chemical Property Estimation Methods: Environmental Behavior of Organic Compounds. McGraw-Hill Book Co., New York.

MAROCHINI, A. 1984. Hazardline Data Base, Occupational Health Services, Inc., Secaucus, NJ. (Note: This is a computerized data base on-line through Bibliographic Retrieval Services, Lapham, NY.)

MICROBIOLOGICAL ASSOCIATES, INC. 1986. Subchronic toxicity of methyl isobutyl ketone in Sprague-Dawley rats. Office of Solid Waste, U.S. Environmental Protection Agency (USEPA). Washington, D.C.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH). 1978. Criteria for a Recommended Standard--Occupational Exposure to Ketones. Washington, D.C. DHEW Publication No. (NIOSH) 78-173.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH). 1983. Registry of Toxic Effects of Chemical Substances. Data Base. Washington D.C. October 1983.

PAVLOU, S.P. 1980. Thermodynamic Aspects of Equilibrium Sorption of Persistent Organic Molecules at the Sediment-Seawater Interface: A Framework For Predicting Distributions in the Aquatic Environment. IN: Contaminants and Sediments. Volume 2. Baker, R.A. (Editor). Science Publishers, Inc. Ann Arbor, MI.

TDB PEER REVIEW COMMITTEE. 1984. Toxicology Data Bank, National library of Medicine and National Institutes of Health, Department of Health and Human Services, Washington, D.C. (Computerized Data Base).

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1986. Risk Reference Dose for Methyl Isobutyl Ketone. Integrated Risk Information System (IRIS). [Note: This is an EPA computerized database.]

VERSCHUEREN, K. 1977. Handbook of Environmental Data on Organic Chemicals. Van Nostrand Reinhold Co., New York. 659 pages.

WEAST, R.E., ed. 1981. Handbook of Chemistry and Physics. 62nd ed. CRC Press, Cleveland, Ohio. 2332 pages.

METHYL MERCURY/DIMETHYL MERCURY[1/]

Summary

Methyl mercury compounds (mono- and dimethyl) affect primarily the central nervous system (sensory-motor) and kidneys following acute and chronic exposures. Methyl mercury compounds are effectively absorbed following oral exposures and readily pass through the blood brain barrier and the placenta. Some positive indications of mutagenicity for methyl mercury have been observed *in vivo* with *Drosophila*, and *in vitro* with mammalian cell cultures. Dimethyl mercury did not cause visible damage to human chromosomes in an *in vitro* test. DNA damage following exposure of microorganisms to dimethyl mercury has also been reported. Kidney tumors have occurred in mice chronically exposed to methyl mercury.

Data on dimethyl mercury and the chloride salt of monomethyl mercury are presented below.

CAS Number: 115-09-03 [mono-]
593-74-8 [di-]

Chemical Formula: CH_3ClHg [mono-]
CH_3HgCH_3 [di-]

1/ Compiled from the following primary sources:

U.S. Environmental Protection Agency (USEPA). 1984. Mercury Health Effects Update. Health Issue Assessment. Office of Health and Environmental Assessment. Washington, D.C. EPA-600/8-84-019F.

U.S. Environmental Protection Agency (USEPA). 1984. Health Effects Assessment for Mercury. Environmental Criteria and Assessment Office, Cincinnati, Ohio. September 1984. ECAO-CIN-H042 (Final Draft).

World Health Organization (WHO). 1976. Environmental Health Criteria 1. Mercury. World Health Organization, Geneva, Switzerland.

IUPAC Name: Methyl mercuric chloride
Dimethyl mercury

Important Synonyms and Trade Names: Mercury methylchloride; methylmercury chloride; monomethyl mercury

Chemical and Physical Properties

Molecular Weight: 251.1 [chloride salt, mono-] (Sax 1979)
230.67 [di-]

Melting Point: 170°C [chloride salt, mono-] (Sax 1979)

Boiling Point: 92°C at 740 mm Hg [di-] (Merck 1983)
96°C [di-] (Jordan 1954)

Specific Gravity: 4.063 [chloride salt, mono-] (Sax 1979)
3.069 [di-] (Sax 1979)

Solubility in Water: Insoluble (Merck 1983; WHO 1976)

Solubility in Organics: Soluble in ether, alcohol (Merck 1983)

Log Octanol/Water Partition Coefficient (K_{ow}): 2.59 [di-] (Jow and Hansch 1984)

Soil/Water Partition Coefficient: Not Applicable

Vapor Pressure: 63.9 mm Hg at 25°C [di-] (Jordan 1954)

Transport and Fate

Quantitative data on the volatility of monomethyl mercury was not located; however, dimethyl mercury is quite volatile (USEPA 1984a). In the atmosphere, volatile organometals such as dimethyl mercury are unstable as the metal-carbon bonds are susceptible to homolytic

cleavage by light (USEPA 1984a). Dimethyl mercury is also subject to removal by rainfall. In acidic rainwater, dimethyl mercury is converted to monomethylmercury which is then returned to the earth to cycle again.

Methylation of ionic mercury in the environment can occur under a variety of conditions including in aerobic and anaerobic waters, in sediments, in the presence of anaerobic and aerobic microbes and in freshwater bodies such as eutrophic and oligotrophic lakes (USEPA 1984a). The mechanism of synthesis of methyl mercury compounds from inorganic mercury (Hg^{++}) most likely involves the non-enzymatic methylation of mercuric mercury ions by methylcobalamine compounds (Vitamin B_{12}) that are produced as a result of bacterial synthesis (USEPA 1984a). The formation of dimethyl mercury is favored by high pH whereas formation of monomethylmercury is favored by a low pH environment (WHO 1976). It is hypothesized that dimethyl mercury synthesized in this fashion diffuses from aquatic environments to the atmosphere (WHO 1976).

Little methyl mercury is found in sediments because the conversion of inorganic mercury to an organic form results in desorption from sediment particles at a fast rate. Strains of bacteria capable of methylating mercury have been isolated from soil, water and marine sediments (USEPA 1984a). Bacteria are also capable of demethylating methyl mercury compounds and of splitting the carbon-mercury bond in a variety of other organic mercurials. This process involves first, the cleavage of carbon-mercury bonds to release Hg^{++} and second, the reduction of Hg^{++} to Hg° which is volatile. These microorganisms occur in both aquatic sediments and soils (USEPA 1980).

The aquatic food chain is the main source of human exposure to methyl mercury compounds (USEPA 1984a). The short-chain alkylmercurials, especially methyl mercury are rapidly bioaccumulated by most aquatic biota and attain highest concentrations in the tissues of large carnivorous fish (USEPA 1984a). In freshwater, reported bioconcentration factors of methyl mercury (as methylmercuric-

chloride) in rainbow trout (Salmo gairdneri) range from 1,000 to 85,700 and from 11,000 to 23,000 in the brook trout (Salvelinus fontinalis) (USEPA 1984b).

Health Effects

Most health effects data reported below are not specific for mono- and dimethyl mercury compounds. In some cases data may be specific for the chloride salt of methyl mercury, chloromethylmercury. Alkyl mercurials have very high toxicity and exposure commonly causes skin burns and other forms of irritation (Sax 1979). They can be absorbed through the skin and are efficiently absorbed from the GI tract (Dale 1972; WHO 1976). Available data from man and experimental animals indicates that the carbon-mercury bond is not broken in vivo to a significant extent. Therefore, most alkyl mercury which enters the body is also excreted as alkyl mercury (Gage 1964; Berglund and Berlin 1969). Alkyl mercury compounds in the body are largely bound to sulfyldryl groups or other ligands of amino acids (Dale 1972). In humans, methyl mercury passes through the blood brain barrier and the placenta very rapidly, in contrast to inorganic mercury compounds. Major target organs are the central nervous system, and the kidney. Methyl mercury destroys neuronal cells in areas of the central nervous system concerned with sensory and motor functions (USEPA 1984a). Clinical symptoms also suggest damage to the peripheral nerves, but histopathological evidence is lacking (USEPA 1984b). Methyl mercury is particularly hazardous because of the difficulty of eliminating it from the body. In experimental animals, organic mercury compounds can produce toxic effects in the gastrointestinal tract, pancreas, liver, heart, and gonads, with involvement of the endocrine, immunocompetent, and central nervous systems.

Prenatal life is the most sensitive stage of the life cycle to methyl mercury (USEPA 1984a). In a documented case of prenatal maternal exposure, the resulting infant exhibited seizures, was hypotonic, irritable, grossly retarded and cortically blind (NAS 1977). Victims (infants, adults) of Minamata disease (methyl mercury

poisoning) exhibit a variety of common symptoms including mental disturbances, ataxia, impairment of the gait, speech disturbances, disturbance in chewing and swallowing, involuntary movement and salivation.

In experimental animals, oral exposure to methyl mercury has been reported to cause embryotoxic and teratogenic effects (USEPA 1984C). In this regard, neurological effects are most common; however, an increased incidence of cleft palate was reported in mice (USEPA 1984b). Varma et al. (1974) report that male Swiss mice injected intraperitoneally with 50 mg/kg dimethyl mercury exhibited reduced fertility as indicated by a decreased mean litter size following pairing with untreated females. Researchers also reported that genetic damage occurred in spermatozoa and spermatids of exposed rats (postmeiotic stages of spermatogenisis) (Varma et al. 1974).

Chromosomal aberrations were detected in Drosophila melanogaster following oral administration of chloromethyl mercury at 1,560 µg/liter and in cultures of human leukocytes and lymphocytes exposed to chloromethyl mercury at concentrations of 200 µmole/liter and 1 µmole/liter, respectively, (NIOSH 1983). Inhibition of DNA synthesis occurred in cultured mouse lymphocytes at 1 µmole/liter chloromethyl mercury (NIOSH 1983). No visible damage to chromosomes was observed in metaphase cultures of cells from human whole blood following addition of 10, 30, and 50 µg/ml medium. Damage to DNA including strand breaks and crosslinks was observed in microogranisms (unspecified, NIOSH 1983) exposed to a concentration of 600 mg/liter dimethyl mercury. Little data on the carcinogenicity of monomethylmercury, chloromethyl mercury or dimethyl mercury were located; however, in one study, mice administered 668 mg/kg chloromethyl mercury for 53 weeks developed a statistically significant increase in the incidence of kidney tumors (NIOSH 1983).

The acute oral LD_{50} of chloromethyl mercury in mice is 57.6 mg/kg and 21 mg/kg in guinea pigs (NIOSH 1983). The intraperitoneal LD_{50} value for dimethyl mercury in male mice is 37.5 mg/kg (Varma et al. 1974).

Toxicity to Wildlife and Domestic Animals

The toxicology database for mercury suggests that divalent inorganic mercury and monomethylmercury (methyl mercury) are the forms which are most hazardous to aquatic systems (USEPA 1980). In freshwater, the acute LC_{50} for methyl mercury (as methyl mercuric chloride) ranges from 65 to 84 µg/liter (USEPA 1984C).

No data on the toxicity of monomethylmercury or dimethyl mercury to terrestrial wildlife or domestic animals was located in available literature.

Regulations and Standards

Ambient Water Quality Criteria (USEPA 1986a)[1/]:

Aquatic Life (Freshwater)

Acute toxicity: 2.4 µg/liter
Chronic toxicity: 0.012 µg/liter

Aquatic Life (Saltwater)

Acute toxicity: 2.1 µg/liter
Chronic toxicity: 0.025 µg/liter

Human Health

Criterion: 144.0 ng/liter

1/ Criteria are for total mercury

ACGIH Threshold Limit Values: TWA[1/] = 0.01 mg/m^3 (alkyl compounds)
STEL[2/] = 0.03 mg/m^3 (alkyl compounds)
TWA = 0.1 mg/m^3 (alkyl and inorganic compounds)

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

For methyl mercury, the D_T value is derived from the same data used by EPA to derive the current Risk Reference Dose (RfD) (USEPA 1986b). This same RfD will also be used as the D_T basis for dimethyl mercury as other toxicity data specific for dimethyl mercury are not available. The RfD is based on the observation that the earliest effects in man are usually observed at blood concentrations of methyl mercury between 200 and 500 mg Hg/ml for both pre- and postnatal exposures. Blood concentrations correspond to body burdens in the range of 30-50 mg Hg/70 kg (WHO 1976), and are equivalent to intakes in the range of 3-7 µg/kg/day (WHO 1976). The Low-Observed-Adverse-Effect-Level (LOAEL) is associated with central nervous system effects such as ataxia and paresthesia (USEPA 1986b). An Uncertainty Factor (UF) of 10 is used by EPA to address the use of a LOAEL in place of a No-Observed-Adverse-Effect-Level (NOAEL) (10). As the effects are seen in sensitive individuals for chronic exposures, no additional factors were deemed necessary by EPA. Derivation of the D_T (RfD) for methyl mercury is as follows:

1/ Time Weighted Average

2/ Short-Term Effect Level

$$D_T = \frac{\text{LOAEL (mg/kg/day)}}{UF}$$

$$= \frac{0.003}{10}$$

$$= 0.0003 \text{ mg/kg/day}$$

REFERENCES

BERGLUND, F. AND B. BERLIN. 1969. Risk of methylmercury cumulation in man and mammals and the relation between body burden of methyl mercury and toxic effects. Chemical Fallout (Miller, M.W. and G.G. Berg, eds.) Springfield, Ill. (Cited in Dale 1972.)

CASARETT and DOULL'S TOXICOLOGY. 1980. The Basic Science of Poisons. Second Edition. Doull, J., Klaassen, C.D., and Amdur, M.O. (Editors). Macmillan Publishing Company, Inc., New York. 778 pp.

DALE, L.G. 1972. The Neurotoxicity of Alkyl Mercury Compounds. The American Journal of Medicine. 53:219-232.

GAGE, J.C. 1964. Distribution and excretion of methyl and phenyl mercury salts. Brit. J. Industr. Med. 21:197-203.

JORDAN, E.T. 1954. Vapor Pressure of Organic Chemicals. Interscience Publishers, Inc. New York, NY. In: The Information System for Hazardous Organics in Water (ISHOW). Dimethyl Mercury. Accession No. 309967. [Note: This is a computerized data base available on the Chemical Information System.]

JOW, P. and C. HANSCH. 1984. Unpublished results for Dimethyl mercury reported in the Information System for Hazardous Organics in Water (ISHOW). Accession No. 309970. [Note: This is a computerized data base available on the Chemical Information System.]

KASPUTIS, D., R.L. NEU and L.I. GARDNER. 1972. Lack of Damage to Human Chromosomes and Dimethyl Mercury. Arch. Environ. Health. 24:378.

NATIONAL ACADEMY OF SCIENCES (NAS). 1977. Drinking Water and Health. Volume I. National Academy of Sciences. Washington, D.C. 939 pp.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NISOH). 1983. Registry of Toxic Effects of Chemical Substances. Volumes I - III. U.S. Department of Health and Human Services. Cincinnati, Ohio. PB85-218071.

SAX, I.N. 1979. Dangerous Properties of Industrial Materials, Fifth Edition. Van Nostrand Reinhold Company, New York.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1980. Ambient Water Quality Criteria for Mercury. Office of Water Regulations and Standards, Criteria and Standards Division. Washington, D.C. EPA-440/5-80-058. October 1980.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1984a. Mercury Health Effects Update. Health Issue Assessment. Final Report. Office of Health and Environmental Assessment. Washington, D.C. EPA-600/8-84-019F.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1984a. Mercury Health Effects Update. Health Issue Assessment. Final Report. Office of Health and Environmental Assessment. Washington, D.C. EPA-600/8-84-019F. August 1984.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1984b. Ambient Water Quality Criteria For Mercury. Office of Water Regulations and Standards. Criteria and Standards Division. Washington, D.C. EPA-440/5-84-026.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1984c. Health Effects Assessment for Mercury. Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office. Cincinnati, OH. EPA-540/1-84-042. September 1984.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1986a. Quality Criteria for Water, 1986 ("The Gold Book"). Office of Water Regulations and Standards, Washington, DC. EPA 440/5-86-001.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1986b. Risk Reference Dose for Methyl Mercury. Integrated Risk Information System (IRIS). [Note: This is an EPA computerized data base.]

VARMA, M.M., E.L. DAGE and S.R. JOSHI. 1974. Mutagenicity Following Administration of Dimethyl Mercury in Swiss Mice. J. Environ. Sys. 4(2):135-142.

WORLD HEALTH ORGANIZATION (WHO). 1976. Environmental Health Criteria 1. Mercury. World Health Organization. Geneva, Switzerland. 131 p.

N-NITROSODIMETHYLAMINE[1/]

Summary

N-Nitrosodimethylamine (NDMA) was carcinogenic in all animal species tested, inducing benign and malignant tumors by various routes. NDMA has been determined to be mutagenic (activated preparations) in bacterial and mammalian test systems. Systemic effects of exposure to NDMA include primarily liver and kidney damage. NDMA is an eye irritant and direct contact causes corneal damage.

CAS Number: 62-75-9

Chemical Formula: $C_6H_6N_2O$

IUPAC Name: N,N-Dimethylnitrosamine

Important Synonyms and Trade Names: dimethylnitrosamine; NDMA; DMNA

Chemical and Physical Properties

Molecular Weight: 74.1 (Merck 1983)

Boiling Point: 152°C (Weast 1977)

Specific Gravity: 1.005 (Merck 1983)

1/ Compiled from: United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL). 1985. Physical, Chemical, and Toxicological Data Summaries of 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

Also: U.S. Environmental Protection Agency (USEPA). 1980. Ambient Water Quality Criteria for Nitrosamines. Office of Water Regulations and Standards, Criteria and Standards Division, Washington, D.C. EPA 440/5-80-064. NTIS No. PB81-117756.

Solubility in Water: 1,000 g/liter (USEPA 1985) (infinitely water soluble)

Solubility in Organics: Soluble in alcohol and ether (Merck 1983)

Log Octanol/Water Partition Coefficient (K_{ow}): -0.57 (Hansch and Leo, 1979)

Soil/Water Partition Coefficient (K_{oc}): Not Applicable

Bioconcentration Factor: Not Applicable

Vapor Pressure (mm Hg): 8.1 mm Hg at 20-30°C (USEPA 1985)

Henry's Law Constant: Not Applicable

Transport and Fate

The high vapor pressure of N-Nitrosodimethylamine (NDMA) indicates that volatilization will be an important transport process. The subsequent chemical fate of NDMA in the atmosphere is unknown. However, studies of aqueous solutions of NDMA suggest that photolysis does occur. It therefore seems likely that NDMA released to the air could photolyze in the presence of water vapors present in the atmosphere.

In aqueous solutions ranging in pH from 8-11, half-lives of 7-18 hours were observed (Polo and Chow, 1976) as compared with 4 hours in distilled water, and 1 hour or less in more acidic solutions. Under alkaline conditions, breakdown products of NDMA are dimethylamine, N_2O and N_2; under more acidic conditions, HNO_2 is formed, which can then react with dimethylamine to reform nitrosodimethylamine. NDMA is not hydrolyzed to an appreciable extent (Polo and Chow 1976; USEPA 1979).

Little sorption of NDMA to soils is expected to occur given its high solubility in water. The combined low organic partionining and high water solubility indicate that NDMA will be a mobile environmental

contaminant. Leaching studies by Dean-Raymond and Alexander (1976) indicated that NDMA exhibits characteristics similar to chloride ion, and therefore it is not likely to be retained on soil. Slow breakdown by sewage microorganisms has been reported (USEPA 1979).

Some uptake of NDMA in lettuce and spinach grown in hydroponic solutions containing soil, sand or just water was reported by Dean-Raymond and Alexander (1976). Two days following the addition and equilibration of NDMA to concentrations of 10 or 100 mg/liter, samples (leaves) were analyzed for NDMA content. Lettuce grown in sand had concentrations of 1.38 mg/kg dry weight and 14.4 mg/kg dry weight at 10 and 100 mg/liter concentrations, respectively. Lettuce grown in soil at a concentration of 100 mg/liter contained 106 mg/kg dry weight tissue. Spinach grown only in water contained 0.54 mg/kg dry weight and 5.6 mg/kg dry weight at concentrations of 10 and 100 mg/liter, respectively. Under natural conditions, however, NDMA is not commonly found in plants (USEPA 1980).

Bioconcentration data for NDMA were not located in available literature. However, given the high aqueous solubility and low organic partitioning behavior, bioconcentration would not be expected to occur.

Health Effects

NDMA is very irritating to the eyes. Direct contact causes corneal damage. Systemic effects include liver and kidney damage (OHS 1985). Symptoms of exposure include nausea, headache, vomiting, abdominal cramps, diarrhea, fever, weakness, jaundice and liver enlargement.

NDMA and other N-nitroso compounds are acutely toxic to both animals and humans (USEPA 1980). In experimental animals, acute exposure to NDMA produced liver lesions within 24-48 hours; death occurred typically in three to four days (USEPA 1980). Other injuries included peritoneal and plural exudates containing high proportions of blood (USEPA 1980).

In humans, exposure to NDMA results in liver damage. Necropsy of at least one victim of acute NDMA exposure revealed liver cirrhosis with regenerating nodules. Another acutely exposed subject died of bronchopneumonia.

Nitrosamines have been shown to be embryotoxic and teratogenic when administered to rats late in pregnancy; unlike nitrosamides which exhibit teratogenic effects early in pregnancy (USEPA 1980). Nitrosamines are mutagenic in test systems following metabolic activation. For example, liver microsomal preparations from mouse, rat, hamster and man are capable of activating nitrosamines. Microsomal preparations from organs other than the liver have been shown to be ineffective in activating nitrosamines to mutagens in bacterial systems (USEPA 1980). NDMA has been reported to induce forward/reverse mutation in several bacterial species, gene recombination and conversion in Saccharomyces cerevisiae, recessive lethal mutation in Drosophila melanogaster and chromosome aberrations in mammalian cells (USEPA 1980). Positive results were achieved in recently completed chromosome aberration tests (National Toxicology Program 1986) in Chinese hamster ovary cells. Sister chromatid exchanges were also observed in this same test system (National Toxicology Program 1986). NDMA was carcinogenic in all animal species tested, inducing both benign and malignant tumors by various routes (OHS 1985).

The acute oral LD_{50} in rats is 26 mg/kg. The acute inhalation LC_{50} values in rats and mice are 78 ppm/4 hr and 57 ppm/4 hr, respectively (OHS 1985).

Toxicity to Wildlife and Domestic Animals

NDMA has been shown to cause heptacellular carcinomas in rainbow trout chronically fed contaminated diets (200-800 mg/kg) (USEPA 1980). Crayfish exposed for six months to NDMA exhibited extensive degenerations in the antennal gland at 200,000 µg/liter and hyperplasia of tubular cells in the hepatopancreas at 100,000 µg/liter NDMA (USEPA 1980). The acute values for freshwater species Daphnia magna and the bluegill are 7,760 and 5,850 µg/liter, respectively.

The acute low oral lethal dose in dogs (LD_{LO}) is 20 mg/kg. The acute low inhalation concentration in dogs (LC_{LO}) is 16 ppm/4 hr (OHS 1985). The acute oral LD_{50} in hamsters is 28 mg/kg.

Regulations and Standards

Ambient Water Quality Criteria (USEPA 1986)[1/]:

The available data are inadequate for establishing specific criteria. However, EPA does report the lowest values known to be toxic in aquatic organisms:

Aquatic Life (Freshwater):

Acute Toxicity: 5,850 µg/liter
Chronic Toxicity: No data available

Aquatic Life (Saltwater):

Acute Toxicity: 3,300 mg/liter
Chronic Toxicity: No data available

Human Health:

Due to the carcinogenicity of N-nitrosodimethylamine the ambient water criterion in set at zero. Estimates of the carcinogenic risks associated with lifetime exposure from ingestion of contaminated water and contaminated aquatic organisms are:

1/ Criteria are for "nitrosamines".

Risk	Concentration
10^{-5}	8.0 mg/liter
10^{-6}	0.8 mg/liter
10^{-7}	0.08 mg/liter

CAG Potency Slope for Oral Exposure[1/] (USEPA 1985): 25.9 $(mg/kg/day)^{-1}$

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

For carcinogens such as N-nitrosodimethylamine, the D_T value is based on the USEPA Cancer Assessment Group's cancer potency slopes. The cancer potency slopes have been estimated for oral exposure routes and for inhalation exposure for some chemicals. The slopes are intended to be a plausible upper bound of the potency of a carcinogen in inducing cancer at low doses. Calculation of a D_T using a cancer potency slope requires selection of an acceptable cancer risk level. A range of risk levels from 10^{-4} to 10^{-7} is considered for all carcinogens, therefore a range of D_T values is presented. Derivation of the D_T values for N-nitrosodimethylamine is as follows:

$$D_T = \frac{\text{Risk Level}}{\text{Potency Slope } (mg/kg/day)^{-1}}$$

$$= \frac{1 \times 10^{-4}}{25.9\ (mg/kg/day)^{-1}}$$

$$= 3.86 \times 10^{-6}\ mg/kg/day$$

1/ The potency factor presented has not been derived by the linear multi-stage model typically used by EPA to determine carcinogenic potency. Rather, a time-to-tumor model was utilized by EPA instead. The potency factor derived from this derivation is reported (see USEPA 1980).

The range of D_T values for N-Nitrosodimethylamine is presented below:

Risk Level	D_T (mg/kg/day)
10^{-4}	3.86×10^{-6}
10^{-5}	3.86×10^{-7}
10^{-6}	3.86×10^{-8}
10^{-7}	3.86×10^{-9}

References

ASTM. 1985. Standard Practice for conducting bioconcentration tests with fishes and saltwater bivalve mollusca. Designation E 1022-84, pages 590-62. In: 1985 Annual Book of ASTM Standards Volume 11.04. American Society for Testing and Materials, Philadelphia, Pennsylvania.

DAVIES, R.P. and DOBBS, A.J. 1984. The prediction of bioconcentration in fish. Water Res. 18(10): 1253-1262.

DEAN-RAYMOND, D. and ALEXANDER, M. 1976. Plant uptake and leaching by dimethylnitrosamine. Nature, 363:394-395.

HANSCH, C. and A.J. LEO. 1979. Substituent constants for correlation analysis in chemistry and biology. John Wiley and Sons, New York, NY.

KADEG, R.D., PAVLOU, S.P., DUXBURY, A.S. 1986. Elaboration of Sediment Normalization Theory for Non Polar Hydrophobic Organic Chemicals. U.S. Environmental Protection Agency, Criteria and Standards Division, Washington D.C.

KENAGA, E.E. and GORING, C.A.I. 1980. Relationship Between Water Solubility, Soil Sorption, Octanol-Water Partitioning and Concentration of Chemicals in Biota. In: Aquatic Toxicology, ASTM STP 707. J.G. Eaton, P.R. Parrish, and A.C. Hendricks (Eds.). American Society for Testing and Materials, pp. 78-115.

LYMAN, W.J., LORETTI, C.P. 1986. Prediction of Soil and Sediment Sorption for Organic Compounds (Comment Final Draft). U.S. Environmental Protection Agency, Monitoring and Data Support Division, Office of Water Regulations and Standards. Washington D.C.

LYMAN, W.J., W.F. REEHL and D.H. ROSENBLATT. 1982. Handbook of Chemical Property Estimation Methods: Environmental Behavior of Organic Compounds. McGraw-Hill Book, Co., New York, NY.

MAGEE, P.N. et al. 1976. N-nitroso Compounds and Related Carcinogens. IN: USEPA 1980 Ambient Water Quality Criteria for Nitrosamines. Office of Water Regulations and Standards, Criteria and Standards Division, Washington, D.C. EPA 440/5-80-064. NTIS No. PB81-117756.

NATIONAL TOXICOLOGY PROGRAM (NTP). 1986. Fiscal Year 1986 Annual Plan. U.S. Department of Health and Human Services, Public Health Service. Washington, D.C. NTP-86-086. May 1986.

OCCUPATIONAL HEALTH SERVICES, INC. (OHS). 1985. Hazardline Data Base. [Note: This is a computerized data base.]

POLO, N. and CHOW, Y.L. 1976. Efficient photolytic degradation of nitrosamines. Journal NCI, 56:997-1001.

THE MERCK INDEX. 1983. An Encyclopedia of Chemicals, Drugs and Biologicals. Tenth ed. Windholz, M., Budavan, S., Blumetti, R.F. and Otterbein, E.S. (eds.). Merck and Company, Inc., Rahway, New Jersey.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1979. Water-Related Environmental Fate of 129 Priority Pollutants. Washington D.C. December 1979. EPA 440/4-79-029.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1980. Ambient Water Quality Criteria for Nitrosamines. Office of Water Regulations and Standards, Criteria and Standards Division, Washington, D.C. EPA 440/5-80-064. NTIS No. PB81-117756.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1985. Draft Superfund Public Health Evaluation Manual. Prepared by ICF Incorporated, Washington, D.C. USEPA Office of Solid Waste and Emergency Response, Washington, D.C. EPA Contract No. 68-01-7090.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1986. Quality Criteria for Water, 1986 ("The Gold Book"). Office of Water Regulations and Standards, Washington, DC. EPA 440/5-86-001.

1,4-OXATHIANE[1/]

1,4-Oxathiane is a volatile and water soluble heterocyclic compound. No data on the toxicity of 1,4-oxathiane to humans was located in available literature. Additionally, no information on the subchronic, chronic or reproductive toxicity of oxathiane in animals or data on the mutagenicity or carcinogenicity were located. The acute oral LD_{50} values in male and female rats are 3,328 and 3,000 mg/kg, respectively.

CAS Number: 15980-15-1

Chemical Formula: $O(CH_2CH_2)S$

IUPAC Name: 1,4-Thioxane

Important Synonyms and Trade Names: Thioxane

Chemical and Physical Properties

Molecular Weight: 104.1 (Sax 1979)

Boiling Point: 148.7°C (Sax 1979)

Melting Point: -17°C (Buckingham 1982)

Specific Gravity: 1.11 (Berkowitz et al., 1978)

Solubility in Water: 20,000 mg/l

1/ Compiled from: United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL), 1985. Physical, Chemical, and Toxicological Data Summaries for 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

Log Octanol/Water Partition Coefficient (K_{ow}): -0.16 (Lyman et al. 1982) Fragment Method

Soil/Water Partition Coefficient (K_{oc}): Not Applicable

Bioconcentration Factor: Not Applicable

Vapor Pressure (mm Hg): 5.1 mm Hg at 25°C (Merck 1983)
3.9 mm Hg at 20°C (Berkowitz et al. 1978)

Henry's Law Constant: Not Applicable

Transport and Fate

The vapor pressure of oxathiane indicates that volatilization from environmental media is likely to be a major transport pathway. However, the very high water solubility of oxathiane will likely offset appreciable volatilization (Berkowitz et al., 1978). No data was available on the chemical fate of oxathiane in water or air. Little sorption of oxathiane to soils is expected to occur given its high solubility in water. The combined low organic partitioning and high water solubility suggest that oxathiane will be a mobile environmental contaminant.

Bioconcentration data were not located for oxathiane in available literature. However, given the high aqueous solubility and low organic partitioning behavior, bioconcentration would not be expected to occur. Data on the persistence of 1,4-oxathian were not located in available literatre.

Health Effects

No data on the toxicity of 1,4-oxathiane to humans was located in available literature. The acute lethality values (LD_{50}) for oxathiane in groups of male rats was 3,328 mg/kg (Mayhew and Muni 1986). No acute LD_{50} could be computed for female rats. The combined LD_{50} value for both sexes was 3,123 mg/kg based on an

estimated female LD_{50} of 3,000 mg/kg (Mayhew and Muni 1986). Antemortem observations included: coma, polypnea, lacrimation, dyspnea, lethargy, ataxia, cyanosis, squinted eyes, epistaxis, wheezing, decreased body temperature, piloerection, hunched posture and alopecia. Necropsy of animals which died revealed discolored intestines and intestinal contents of nearly all animals. Additionally, gaseous stomachs or intestines, discolored stomach contents and distended and discolored urinary bladders were seen in some animals (Mayhew and Muni 1986).

Exposure to undiluted oxathiane resulted in slight skin irritation and moderately severe eye irritation in rabbits (Berkowitz et al. 1978).

Toxicity to Wildlife and Domestic Animals

No data was located in available literature.

Regulations and Standards

None Located.

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

For 1,4-oxathiane, the D_T value is derived from an acute oral LD_{50} value in rats (Mayhew and Muni 1986). The D_T value is computed as the product of the acute value and an interim application factor of 1×10^{-5} (Layton et al. 1986). The application factor allows the derivation of an acceptable long-term intake rate (D_T) based on the results of acute tests in the absence of more suitable long-term studies (i.e., chronic studies). The application factor

corresponds to the cumulative percentile on a lognormal distribution of NOEL/LD_{50} ratios for various chemicals. The percentile was chosen to reduce the probability that the calculated dose rate would be above a toxic level; the 5th cumulative percentile was used by Layton et al. (1986) and was found to be equal to 10^{-3}. The application factor also includes a safety factor of 100 to address interspecies and intraspecies variability; therefore, an interim estimate of D_T is obtained when the application factor is multiplied by the acute value. Derivation of this D_T value is as follows:

$$D_T = \text{Acute } LD_{50} \times \text{Application Factor}$$
$$= 3{,}000 \text{ mg/kg/day} \times 1 \times 10^{-5}$$
$$= 0.03 \text{ mg/kg/day}$$

REFERENCES

BERKOWITZ, J.G., GOYER, M.M., HARRIS, J.C., LYMAN, W.J., HORNE, R.A., NELTEN, L.H., HARRISON, J.E., and ROSENBLATT, D.H. 1978. Literature Review--Problem definition studies on selected chemicals. Final Report. Vol. II. Chemistry, toxicology, and potential environmental effects of selected organic pollutants. Contract No. DAMD 17-77-C-7037, Arthur D. Little, Inc. Cambridge, MA (AD B052946L).

BUCKINGHAM, J., Executive Editor. 1982. Dictionary of Organic Compounds. Volume IV. Chapman and Hall, New York, NY, P. 4428.

LAYTON, D.W., MALLOU, B.J., ROSENBLATT, D.H. and SMALL, M.J. 1986. Deriving Allowable Daily Intakes For Systemic Toxicants Lacking Chronic Toxicity Data. Regulatory Toxicology and Pharmacology. In Press.

LYMAN, W.J., W.F. REEHL AND D.H. ROSENBLATT. 1982. Handbook of Chemical Property Estimation Methods: Environmental Behavior of Organic Compounds. McGraw-Hill Book Co., New York, NY.

MAYHEW, D.A. and MUNI, I.A. 1986. Dermal, Eye and Oral Toxicologic Evaluations: Phase II Report: Acute Oral LD50 Determinations of Benzothiazole, Dithiane and Oxathiane. American Biogenics Corporation, Decatur, IL. Contract No. DAMD17-82-C-2301.

THE MERCK INDEX. 1983. An Encyclopedia of Chemicals, Drugs and Biologicals. Tenth ed. Windholz, M., Budavan, S., Blumetti, R.F. and Otterbein, E.S. (eds.). Merck and Company, Inc., Rahway, New Jersey.

SAX, I.N. 1979. Dangerous Properties of Industrial Materials, Fifth Edition. Van Nostrand Reinhold Company, New York.

PARATHION[1/]

Summary

Parathion, an organophosphorus pesticide, is highly acutely toxic in both animals and humans. The primary mode of toxicity following both acute and chronic exposures is via inhibition of the enzyme acetylcholinesterase in the peripheral and central nervous systems. Parathion has yielded both positive and negative results for mutagenic activity in different test systems. The result of carcinogenicity testing was negative in longterm feeding studies with mice, and equivocal in studies utilizing rats.

CAS Number: 56-38-2

Chemical Formula: $CH_{10}H_{14}NO_5PS$

IUPAC Name: O,O-diethyl O-p-nitrophenyl phosphorothioate

Important Synonyms and Trade Names: Ethyl parathion; phosphorothioc acid O,O-diethyl O-(4-nitrophenyl) ester

Chemical and Physical Properties

Molecular Weight: 291

Melting Point: 6°C (Merck 1983)

Boiling Point: 375°C, (Merck 1983)

Specific Gravity: 1.26 (Merck 1983)

1/ Compiled from: United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL), 1985. Physical, Chemical, and Toxicological Data Summaries for 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

Solubility in Water: 20 mg/liter (Merck 1983)
24 mg/liter (TDB Peer Review Committee 1984)

Solubility in Organics: Soluble in alcohols, esters, ethers, ketones, and aromatic hydrocarbons (Merck 1983)

Log Octanol/Water Partition Coefficient (K_{ow}): 3.81 (Lyman et al. 1982)
3.93 (Briggs 1981)

Soil/Water Partition Coefficient:

600	Briggs (1981) Table III (experimental)
800	Lyman et al. (1982) Eqn 4-5 (S = 22)
3,200	Lyman et al. (1982) Eqn 4-8 (log K_{ow} = 3.9)
3,000	Lyman and Loreti (1986) Eqn I (log K_{ow} = 3.9)
3,500	Lyman and Loreti (1986) Eqn II (log K_{ow} = 3.9)
3,500	Lyman and Loreti (1986) Eqn III (log K_{ow} = 3.9)
3,970	Kadeg et al. (1986) (log K_{ow} = 3.9)

Bioconcentration Factor:

497	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 3.82)
315	Davies and Dobbs (1984) Eqn B (log K_{ow} = 3.87)
463	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 3.81)
571	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 3.93)
108	Davies and Dobbs (1984) Eqn 3 (S = 22)
167	Davies and Dobbs (1984) Eqn A (log K_{ow} = 3.87)
132	Davies and Dobbs (1984) Eqn C (log K_{ow} = 3.9)
328	Davies and Dobbs (1984) Eqn C (log K_{ow} = 3.9)
542	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 3.9)
31-232	USEPA (1986) Experimental Data (Brook trout muscle)
33-201	USEPA (1986) Experimental Data (Fathead minnow whole-body)
27	USEPA (1986) Experimental Data (Bluegill muscle)

Vapor Pressure (mm Hg): 3.78×10^{-5} mm Hg at 20°C (Merck 1983)
0.57×10^{-5} (USEPA 1975)

Henry's Law Constant: 1.1×10^{-6} atm-m^3/mole (calculated)
6.9×10^{-7} atm-m^3/mole (calculated)

Transport and Fate

The vapor pressure of parathion suggests that some losses from environmental media may occur as a result of volatilization. Soil temperatures and moisture content will play a large role in controlling volatilization processes (Mulla et al. 1981).

In water, the persistence of parathion is pH dependent. Parathion is quite stable in waters with pH 1-7 (Mulla et al. 1981). At 10°C and pH 1-5, the half-life of parathion was 1,000 days, while at 70°C under identical pH conditions the half-life was 1.7 days (Muhlman and Schrader, 1977). At higher pHs (i.e., above neutral) hydrolysis of parathion proceeds rapidly (Paris and Lewis, 1973).

Numerous studies have reported parathion persistence in soils for periods ranging from weeks to years (Mulla et al. 1981). Kasting and Woodward (1951) found trace levels of parathion 325 days following its application at 100 lb/acre to a sandy loam soil of pH 6.8. Two lower application rates (2 and 12 lbs) were non-detectable after 16 and 79 days, respectively. Chisholm et al. (1955) reported that 3.2 percent of the initial applied concentration of parathion (15.7 ppm per year/5 years) was still detectable at the end of the fifth year. Chisholm and MacPhee (1972) reported that residues of parathion (0.2 kg/ha) were still detectable 16 years following its application at a rate of 176 kg/ha.

Iwata et al. 1975 report the persistence of parathion in different soil types. In general, over the range of pHs studied (6.7-8.7) persistence was greater in soils having higher organic carbon contents such as clays and silt loams. Persistence (i.e., 50 days following application) ranged from 0.7 ppm parathion in a sandy loam (initial concentration 470 ppm, 0.1 percent organic carbon) to 25 ppm in a windy loam (initial concentration 450 ppm, 10.8 percent organic carbon). In more alkaline soils parathion will be degraded more rapidly, while in acidic soils, persistence will be considerably greater (Mulla et al. 1981).

A range of estimated and experimental soil/water partition coefficients (K_{OC}) is reported above and indicates that sorption of parathion to soils/sediments and dissolved organic material will occur. The combined water solubility and organic partitioning data suggest that parathion will exhibit some degree of environmental mobility.

A range of estimated and experimental bioconcentration factors (BCFs) for parathion is also reported above. ASTM (1985) indicates that chemicals with bioconcentration factors less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. In light of the magnitude of the reported BCF values, it appears that magnification of parathion residues in higher vertebrates may occur.

Health Effects

The principal mode of toxicity of parathion in mammals is through inhibition of the enzyme acetylcholinesterase. Inhibition is increased by the oxidative conversion of parathion to paraoxon *in vivo* (Casarett and Doull 1980). Symptoms of systemic poisoning include chest tightness, wheezing expiration (due to broncho- constriction), salivation, lacrimation, sweating, increased peristalsis, nausea, vomiting, abdominal cramps, diarrhea, bradycardia, frequent and involuntary urination (due to contraction of smooth muscle in the bladder), weakness, dyspnea, and elevated blood pressure (Casarett and Doull 1980).

Rider et al. (1969) administered parathion to prison volunteers at dosages of 0.043, 0.064, 0.086 and 0.11 mg/kg/day (assuming 70 kg reference weight) for between 30 and 42 days. Plasma ChE was inhibited in one subject in the high dose group on day four and in all subjects by day 16. The lower dosages resulted in only slight decreases in plasma ChE activity.

Dogs administered concentrations of 0.021, 0.047, or 0.117 mg/kg/day parathion in their diets for 24 weeks experienced significantly decreased levels of plasma cholinesterase at all dose levels. At the two higher dose levels, plasma cholinesterase was inhibited by 60-70 percent (NAS 1977 cite Frawley and Tuyat 1957). Rats fed parathion for 84 days experienced slight decreases in plasma cholinesterase at levels of 0.04 and 0.06 mg/kg/day. No effect was seen at 0.02 mg/kg/day (NAS 1977 cite Edson 1964). In a study where dogs were administered 1, 2, or 3 mg/kg/day parathion in capsules six days/week for 90 days, the medium dose group (2 mg/kg/day) lived for three weeks and exhibited unspecified signs of toxicity continuously. Animals in the two remaining dose groups survived and exhibited nervous and irritable behavior only during the early stages of treatment. No gross pathology was evident but degenerative liver changes were observed following histopathologic determinations (NAS 1977 cite Hazelton and Holland 1950).

Female rats injected intraperitoneally with 3 or 3.5 mg/kg parathion during day 11 of gestation experienced mortality, an increased number of resorptions, reduced number of fetuses per litter, and reductions in fetal and placental weights (NIOSH 1983). Additionally, twenty-four day-old progeny of female rats administered 0.01, 0.1, or 1.0 mg/kg/day parathion during days 2-15 of gestation experienced reductions in psuedocholinesterase and plasma renin as well as altered electrocardiograms (IARC 1982). Rats given 10, 20 or 50 mg/kg/day parathion over a period of two generations exhibited reduced litter sizes at birth and high postnatal mortality during the first generation at 20 and 50 mg/kg and increased pup mortality at 10 mg/kg in the second generation (IARC 1982). Parathion was embryocidal following its administration to mice on gestational days 12, 13, and 14 (Casarett and Doull 1980).

Chromosomal abnormalities were reported in guinea pigs injected intratesticularly with 0.05 mg parathion (NAS 1977 cite Dikshith 1973). Rats orally administered 10 mg/kg parathion over a period of 28

days exhibited damage to DNA including strand breaks and crosslinks (NIOSH 1983), as did mice at 20 mg/kg (oral) over the same exposure duration. Rats and mice injected intraperitoneally (3 µg/kg parathion) also exhibited DNA strand breaks and crosslinks (NIOSH 1983). Negative results are also reported in various mammalian and bacterial systems including E. coli pol, Salmonella (activated), S. marcescens, S. cerevisiae, Drosophila, W138 human fibroblasts, and a dominant lethal assay in mice exposed via diet or intraperitoneal injection (USAMBRDL 1985). Studies on the carcinogenicity of parathion in mice have not indicated any increase in tumor formation (NIOSH 1983), though in an NCI bioassay utilizing rats the results were considered equivocal.

Parathion is highly acutely toxic in both humans and animals. The lethal dose in humans is 0.24 mg/kg (NIOSH 1983). In rats, the oral LD_{50} is 2 mg/kg, and 6 mg/kg in the mouse (NIOSH 1983). The dermal LD_{50} in mice is 32.4 mg/kg (NIOSH 1983).

Toxicity to Wildlife and Domestic Animals

Parathion is acutely toxic to a variety of freshwater organisms. Immature amphipods (Gammarus spp.) exhibited sensitivity to parathion at concentrations ranging from 0.25 - 0.62 µg/liter. Mature amphipods appeared to be less affected with an LC_{50} of 3.5 µg/liter (USEPA 1986). First instar cladocerans also exhibited high sensitivities to parathion with LC_{50} values ranging from 0.47 - 0.60 µg/liter. Adults were slightly less sensitive, with LC_{50} values ranging from 1.0 - 1.8 µg/liter. The greatest disparity in sensitivity between adults and juveniles occurred in the crayfish (Orconectes nais). An early instar was 375 times more sensitive to parathion than were adults (USEPA 1986). The LC_{50} for the crayfish instar was 0.04 µg/liter. Acute toxicity data for 31 freshwater species indicate that the most sensitive genus, Orconectes is over 130,000 times more sensitive than the most resistant, Tubifex and Limnodrilus, which both had LC_{50}

values of 5,230 µg/liter (USEPA 1986). Fathead minnows (Pimephales promelas) were significantly affected by chronic exposure to parathion at concentrations of 9 µg/liter.

Subchronic toxicity of parathion in some domestic animals has been summarized by NAS (1977). In goats, oral doses of 8 mg/kg/day were lethal following 11 days of administration. Cattle fed parathion in capsules at doses of 0.022 and 0.112 mg/kg/day for 81 days exhibited no noticeable adverse effects. In another study with cattle, 0.11 and 0.89 mg/kg/day were also reported to produce no noticeable adverse effects.

In avian species such as the Japanese quail (Coturnix japonica), parathion (27 ppm) inhibited egg production and resulted in reduced hatchability (Shellenberger et al. 1968). Mallard ducks (Anas platyrhyncos) fed parathion at doses of 10 ppm experienced no adverse effects other than a reduction in mean shell thickness (NAS 1977 cite Mueller and Lochman 1972).

The acute oral LD_{50} value in dogs is 3 mg/kg and 0.93 mg/kg for cats (NIOSH 1983). In rabbits and guinea pigs, the oral LD_{50} values are 10 mg/kg and 8 mg/kg, respectively (NIOSH 1983). In horses, the oral LD_{50} value is 5 mg/kg (NIOSH 1983). For avian species, the acute oral LD_{50} values in pigeons, quail, and ducks are 3 mg/kg, 6 mg/kg, and 2.34 mg/kg, respectively (NIOSH 1983).

Regulations and Standards

Ambient Water Quality Criteria (USEPA 1986)

Aquatic Life (Freshwater)

Acute Toxicity: 0.065 µg/liter
Chronic Toxicity: 0.013 µg/liter

Aquatic Life (Saltwater)

Acute Toxicity: Insufficient Data

Chronic Toxicity: Insufficient Data

Human Health

No criteria established

OSHA Standard: TWA[1/] = 0.1 mg/m^3

ACGIH Standard: STEL[2/] = 0.3 mg/m^3 (skin caution)

IDLH Standard: 20 mg/m^3

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

For parathion, the D_T value is derived from a subchronic study in humans volunteers fed parathion at dosages of 0.043, 0.064, 0.086, or 0.11 mg/kg/day (Rider et al. 1969). The exposure period ranged from 30-42 days. Plasma ChE was inhibited in all subjects by day 16 in the high dose group, while subjects in the three lower dose groups experienced only slight decreases in plasma ChE activity. Therefore, 0.043 mg/kg/day was identified as a Low-Observed-Adverse-Effect-Level (LOAEL) and was used by NAS 1977 in computing an Acceptable Daily Intake (ADI) for parathion. An Uncertainty Factor (UF) of only 10 was used by NAS (1977), presumably, to address the use of a LOAEL rather than a NOAEL. However, an additional UF of 10 has been included to address the potential for intraspecies variability (sensitive subgroups). Derivation of the D_T for parathion is as follows:

1/ Time Weighted Average.
2/ Short Term Effect Level.

$$D_T = \frac{\text{LOAEL (mg/kg/day)}}{\text{UF}}$$

$$= \frac{0.043}{100}$$

$$= 0.00043 \text{ mg/kg/day}$$

REFERENCES

ASTM. 1985. Standard Practice for conducting bioconcentration tests with fishes and saltwater bivalve mollusca. Designation E 1022-84, pages 590-62. In: 1985 Annual Book of ASTM Standards Volume 11.04. American Society for Testing and Materials, Philadelphia, Pennsylvania.

BRIGGS, G.G. 1981. Theoretical and experimental relationships between soil adsorption, octanol-water partition coefficients, water solubilities, bioconcentration factors, and the parachlor. J. Agric. Food Chem., 29:1050-1059.

CASARETT and DOULL'S TOXICOLOGY. 1980. The Basic Science of Poisons. Second Edition. Doull, J., Klaassen, C.D., and Amdur, M.O. (Editors). Macmillan Publishing Company, Inc., New York. 778 pp.

DAVIES, R.P. and A.J. DOBBS. 1984. The prediction of bioconcentration in fish. Water Res. 18(10):1253-1262.

DIKSHITH, T.S.S. 1973. In vivo effects of Parathion on guinea pig chromosomes. Environ. Physiol. Biochem. 3:161-168.

EDSON, E.T. 1964. No-effect-levels of three organophosphates in the rat, pig, and man. Food Cosmet. Toxicol. 2:311-316.

FRAWLEY, J.P. and FUYAT, H.N. 1957. Effect of low dietary levels of parathion and systox on blood cholinesterase of dogs. J. Agric. Food Chem. 5:346-348.

HAZELTON, L.W. and HOLLAND, E.G. 1950. Pharmacology and toxicology of parathion. Adv. Chem. Series 1(31):31-38.

INTERNATIONAL AGENCY FOR RESEARCH ON CANCER (IARC) WORKING GROUP ON THE EVALUATION OF CARCINOGENIC RISK OF CHEMICALS TO HUMANS. 1982. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans: Volume 30. Miscellaneous Pesticies. IARC, World Health Organization, Lyon, France.

KADEG, R.D., PAVLOU, S.P., DUXBURY, A.S. 1986. Elaboration of Sediment Normalization Theory for Non Polar Hydrophobic Organic Chemicals. U.S. Environmental Protection Agency, Criteria and Standards Division, Washington D.C.

LYMAN, W.J., LORETI, C.P. 1986. Prediction of Soil and Sediment Sorption for Organic Compounds (Comment Final Draft). U.S. Environmental Protection Agency, Monitoring and Data Support Division, Office of Water Regulations and Standards. Washington D.C.

MULLER, H.D. and LOCKMAN, D.C. 1972. Fecundity and progency growth following subacute insecticide ingestion by the mallard. Poultry Science, 51:239-241.

LYMAN, W.J., W.F. REEHL, AND D.H. ROSENBLATT. 1982. Handbook of Chemical Property Estimation Methods: Environmental Behavior of Organic Compounds. McGraw-Hill Book Co., New York, NY.

NATIONAL ACADEMY OF SCIENCE (NAS). 1977. Drinking Water and Health. Volume I. National Academy of Sciences, Washington, DC. pg. 797.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH). 1983. Registry of Toxic Effect of Chemical Substances. Data Base. Washington D.C. October 1983.

RIDER, J.A., MOELLER, H.C., PULETTI, E.J. and SWATER, J.I. 1969. Toxicity of Parathion, Systox, Octamethyl Pyrophosphoramide and Methyl Parathion in Man. Toxicol. Appl. Pharmacol. 14:603-611.

TDB PEER REVIEW COMMITTEE. 1984. Toxicology Data Bank, National library of Medicine and National Institutes of Health, Department of Health and Human Services, Washington, D.C. (Computerized Data Base).

THE MERCK INDEX. 1983. An Encyclopedia of Chemicals, Drugs and Biologicals. Tenth Edition. Rathway, New Jersey, Merck and Company, Inc.

UNITED STATES ARMY MEDICAL BIOENGINEERING RESEARCH AND DEVELOPMENT LABORATORY (USAMBRDL). 1985. Physical, Chemical, and Toxicological Data Summaries for 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1986. Ambient Water Quality Criteria for Parathion. Office of Water Regulations and Standards, Criteria and Standards Division, Washington, D.C. EPA 440/5-86-007. September 1986.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1975. Initial Scientific and Minieconomic Review of Parathion. Office of Pesticide Programs. EPA-540/1-75-001.

SARIN[1/]

Summary

Sarin is a highly toxic chemical formerly manufactured for use as a nerve agent. It is a potent inhibitor of the enzyme acetylcholinesterase in both human and mammalian systems. No data are available on the carcinogenicity of sarin. Sarin did not increase the incidence of dominant lethal mutations in exposed and mated rats; or result in fetotoxicity or teratogenic effects in the same species. It is rapidly broken down in the environment and therefore is not expected to be persistent.

CAS Number: 107-44-8

Chemical Formula: $C_4H_{10}FO_2P$

IUPAC Name: Methylphosphonoflouridic acid 1-methylethyl ester

Important Synonyms and Trade Names: Fluoroisopropoxy methylphosphine oxide; GB; Isopropoxymethylphosphoryl Fluoride

Chemical and Physical Properties

Molecular Weight: 140.09 (Merck 1983)

Melting Point: -57°C (Merck 1983)

1/ Compiled from: Small, M.J. 1984. Compounds Formed From the Chemical Decontamination of HD, GB, and VX and Their Environmental Fate. Technical Report 8304. United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL). Fort Detrick, Frederick, MD. NTIS No. AD-A149515.

Also: Various literature sources cited in the text and referenced in the bibliography.

Boiling Point: 147°C (Merck 1983)

Solubility in Water: Infinitely Soluble (Small 1984)

Log Octanol/Water Partition Coefficient (K_{ow}): 0.72 (Small 1984)

Soil/Water Partition Coefficient (K_{oc}): Not Applicable

Bioconcentration Factor: Not Applicable

Vapor Pressure: 1.57 mm Hg at 20°C (Sax 1979)
2.2 mm Hg at 25°C (DA Pamphlet 1982)

Henry's Law Constant: Not Applicable

Transport and Fate

The vapor pressure of sarin indicates that volatilization from soil surfaces will occur. The chemical fate of sarin released to the air has not been characterized; however, reactions with atmospheric water vapor would likely result in hydrolysis. The immediate sarin hydrolysis product is isopropyl methylphosphonate, which further reacts with water to form methyl phosphonic acid. Hydrolysis of sarin is reported to be quite rapid (Houle et al. 1972, Small 1984). Although reaction rates will decrease with a decrease in temperature, significant hydrolytic decomposition of GB has been reported at -15°C (Shih and Ellen 1984). The water solubility and rapid hydrolytic degradation of sarin indicate that its persistence in environmental media will be low (Houle et al. 1972, Rosenblatt et al. 1975). The persistence of sarin in freshwater is pH dependent and favors more acidic conditions (DA 1982). In one study, at 25°C and a pH of 7, the persistence of sarin was 750 hours vs. 7.5 hours at a pH of 9.0 (DA 1982). The hydrolysis products of sarin (identified above) are more stable; environmental persistence of these products is expected to be greater (Rosenblatt et al. 1975).

Sass et al. (1953) and USATECOM (year unknown) conducted studies on the stability of sarin in soil. In the former study, the percent of applied sarin (0.07 gram) remaining was determined in two soils under two moisture conditions: humus soil (pH 4.5) at 2.9 and 36.8 percent moisture and loam soil (pH 6.5) at 1.4 and 12.8 percent moisture. Samples analyzed at 168 hours post-treatment indicated only 5 percent of the applied sarin remained in the low moisture loam, while no detectable quantities were found in remaining samples. The USATECOM study, utilizing an unspecified soil type containing 1 percent moisture and an initial concentration of 1 mg/g sarin, reported remaining sarin residues of 13 percent, 2.6 percent and 0.02 percent, respectively, at 3, 7, and 35 days post-treatment. Houle et al. (1972) report a rapid loss of applied sarin (100, 1,000 µg/g soil) from three soil types (clay, sandy-clay-loam, sand). At common field conditions of 25°C, 5 percent soil moisture and a windspeed of 4 mph, the predicted half-life of 100 ug sarin/g soil was 2 hours.

Little sorption of sarin in soils is expected to occur given its infinite solubility in water. The rapid rate of hydrolysis for sarin combined with its infinite water solubility indicate that chemical degradation processes will likely predominate over organic partitioning and environmental mobility of the unaltered compound.

Houle et al. (1972) report that sarin applied directly to two types of dry vegetation (cheatgrass, budsage) was lost rapidly through evaporation. Loss of sarin from vegetation was influenced primarily by windspeed. At a windspeed of 4 mph, applied sarin was completely lost in two days. Translocation studies in bean plants (Houle et al. 1972) indicated that a small amount of sarin was absorbed but was lost within a period of 24 hours. Bioconcentration data for sarin were not located in available literature. However, given its infinite aqueous solubility and low organic partitioning behavior, bioconcentration would not be expected to occur.

Health Effects

Sarin is highly toxic and a potent inhibitor of the enzyme acetylcholinesterase in mammalian systems, including humans. The resulting excessive accumulation of acetylcholine results in overstimulation of nerves leading to the respiratory tract, cardiac muscle, gastrointestinal tract, bladder and blood vessels. Death is usually due to respiratory paralysis. Symptoms of exposure include: lacrimation, eye pain, headache, twitching eyelids, chest tightness, salivation, fatigue, weakness, anxiety and anorexia. More severe exposures are characterized by diarrhea, frequent urination, dyspnea, ataxia, convulsions, collapse and paralysis.

The effects of long-term (chronic) overexposure to sarin are not well understood. Some overexposed people have reported experiencing forgetfulness, difficulty in thinking and solving problems, disturbances in vision and persistent muscular aches and pains (DA 1982).

Female rats were mated and exposed to sarin vapor at concentrations of 0.0001 or 0.001 mg/m^3 (Denk 1975). Rats were sacrificed and necropsied at 1, 2, and 3 week intervals while one group was allowed to whelp. Other female rats were given a single intraperitoneal injection (43.8 µg/kg) on the day they were mated or on days 7, 14, and 21 after mating. Rats dosed on day 21 were allowed to whelp while others were sacrificed and necropsied 19 days after mating. No evidence of fetotoxicity or anatomical abnormalities were observed in any of the fetuses examined. In the same study, no evidence of dominant lethal mutations was observed when groups of treated male rats (13.67, 27.34, 54.75, 109.51, and 219.02 µg/kg as a single intraperitoneal injection) were mated with untreated, virgin female rats.

Some compounds structurally similar to sarin have been shown to cause birth defects in animals (DA 1982), however, data specific for sarin are lacking. No data are available on the carcinogenicity or mutagenicity of sarin.

Short-term (acute) exposure to sarin may be fatal at very low doses. The estimated lethal dose for a human is 0.01 mg/kg (Merck 1983). Inhalation LC_{50} values for rats and mice are 3.8 mg/kg (10 minute exposure to 220 mg min/m^3) and 5.4 mg/kg (10 minute exposure to 310 mg min/m^3), respectively (DA 1974). The acute subcutaneous LD_{50} for mice 0.271 mg/kg (Van Meter and Karczman, 1968).

Toxicity to Wildlife and Domestic Animals

Very little data is available on the toxicity of sarin to wild or domestic animals. Inhalation LC_{50} values for guinea pigs, rabbits, cats, dogs, pigs and monkeys are: 3.14 ppm (10 minutes at 180 mg min/m^3); 1.75 ppm (10 minutes at 100 mg min/m^3); 1.05 ppm (10 minutes at 60 mg min/m^3); 0.59 ppm (10 minutes at 34 mg min/m^3); and 1.29 ppm (10 minutes at 74 mg min/m^3) (DA 1974). Sarin is slightly less toxic following dermal exposure as indicated by the LD_{50} values for rabbits, cats, dogs and pigs, respectively: 4.4 mg/kg (depilated); 6.2 mg/kg (depilated); 10.8 mg/kg (depilated) and 115.9 mg/kg (clipped).

Regulations and Standards

The Surgeon General of the United States recommends that pregnant women not be exposed to concentrations of sarin exceeding 0.00003 mg/m^3 averaged over a 72-hour period (DA 1982).

Permissible Exposure Limit (DA 1982): TWA[1/] = 0.0001 mg/m^3

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

1/ Time Weighted Average.

For sarin, the D_T value is based on a developed army standard known as a Control Limit for the General Public (CLGP). The standard was developed by McNamara and Leitnaker (1971) based on data from studies in which animals received single parenteral doses and also from specific inhalation studies of up to six months duration involving concentrations which produced overt toxic effects. The CLGP is also recommended by the Surgeon General of the United States as a limit for exposure of sensitive subgroups such as pregnant women (DA 1982). The CLGP is intended to be protective over an indefinite period when the maximum averaging period for ambient concentrations is 72 consecutive hours.

Derivation of the D_T value from the CLGP standard is accomplished by utilizing an equation developed by Stokinger and Woodward (1958). The equation allows the computation of an Acceptable Daily Intake (ADI or D_T) from a threshold limit value. No Uncertainty Factor (i.e., UF=1) is included in the derivation because 1) the data already address human exposures and 2) the data reflect protection of a sensitive subgroup (i.e., pregnant women). Derivation of the D_T value for sarin utilizing the Stokinger and Woodward equation is as follows:

$$D_T = \frac{TLV \times BR \times d \times A_A}{A_o \times UF \times BW}$$

where:

- TLV = Concentration in air (mg/m^3)
- d = Days of experimental exposure (unspecified, 7days/7days is assumed; therefore d = 1)
- A_A = Efficiency of absorption from air (100 percent assumed)
- A_o = Efficiency of absorption from oral exposure (100 percent assumed)
- UF = Uncertainty Factor
- BR = Breathing Rate (m^3/day)
- BW = Reference Human Body Weight (70 kg)
- D_T = Contaminant intake rate (mg/kg/day)

$$D_T = \frac{0.000003 \text{ mg/m}^3 \times 20 \text{ m}^3\text{/day} \times 1 \times 1}{1 \times 1 \times 70 \text{ kg}}$$

$$= 0.00000086 \text{ mg/kg/day}$$

REFERENCES

ASTM. 1985. Standard Practice for conducting bioconcentration tests with fishes and saltwater bivalve mollusca. Designation E 1022-84, pages 590-62. In: 1985 Annual Book of ASTM Standards Volume 11.04. American Society for Testing and Materials, Philadelphia, Pennsylvania.

DENK, J.R. 1975. Effects of GB on Mammalian Germ Cells and Reproductive Performance. Department of the Army. Headquarters, Edgewood Arsenal. Aberdeen Proving Ground, Maryland. Edgewood Arsenal Technical Report No. EB-TR-74087. AD A006503.

DEPARTMENT OF THE ARMY (DA). 1974. Chemical Data Sheets. Edgewood Arsenal Special Report. Aberdeen Proving Ground, MD. Report Number EO-SR-74001.

DEPARTMENT OF THE ARMY (DA). 1982. Special Occupational Safety and Health Standard for the Evaluation and Control of Occupational Exposure to Agent GB. DA Pamphlet No. 40-8. Headquarters, Department of the Army, Washington D.C.

HOULE, M.J., D.E. LONG, T.D. LEE, N.C. HILL, J.E. MEIKLE ET AL. 1972. The Decay of GB in Environmental Samples (Safest). U.S. Army Test and Evaluation Command. Deseret Test Center. Fort Douglas, Utah. Technical Progress Report No. DTC-PR-73-852.

LYMAN, W.J., W.F. REEHL AND D.H. ROSENBLATT. 1982. Handbook of Chemical Property Estimation Methods: Environmental Behavior of Organic Compounds. McGraw-Hill Book Co., New York, NY.

McNamara, B.P. and F.L. LEITNAKER. 1971. Toxicological Basis for Controlling Emission of GB into the Environment. Department of the Army. Edgewood Arsenal Research Laboratories. Edgewood Arsenal, Maryland. Edgewood Arsenal Special Publication No. EASP 100-98.

ROSENBLATT, D.H., MILLER, T.A., DACRE, J.C., MUUL, I. and COGLEY, D.R. 1975. Problem Definition Studies on Potential Environmental Pollutants. I. Toxicology and Ecological Hazards of 16 Substances at Rocky Mountain Arsenal. Technical Report 7508. U.S. Army Medical Bioengineering Research and Development Laboratory. Fort Detrick, Frederick, MD.

SASS, S., ZENK, T.N. and HILLIARD, R.A. 1953. Stability of Agents in Soils (GA, GB, GD, GF, EA 1211, Paraoxon, EA 1370). CRLR 247. Chemical Corps, Army Chemical Center, MD. In: Small, 1984 (see reference below).

SHIH, M.L. AND R.I. ELLEN. 1984. Stability of aqueous solutions of Sarin and Soman: Influence of concentration and an equation for determining concentrations. Bull. Environ. Contam. Toxicol. 33:1-5.

SMALL, M.J. 1984. Compounds Formed From the Chemical Decontamination of HD, GB, and VX and Their Environmental Fate. Technical Report 8304. United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL). Fort Detrick, Frederick, MD. NTIS No. AD-A149515.

STOKINGER, M.E. AND WOODWARD, A.L. 1958. Toxicological Methods for Establishing Drinking Water Standards. J. Am. Water Works Assoc., 50:517.

THE MERCK INDEX. 1983. An Encyclopedia of Chemicals, Drugs and Biologicals. Tenth Edition. Rahway, New Jersey, Merck and Company, Inc.

UNITED STATES ARMY TEST AND EVALUATION COMMAND (USATECOM) (No Date). Environmental Impact Statement for the Study of the Fate of Agents and Residues in Vegetation and Soil. For USATECOM Project 5-CO-483-000-015. Desert Test Center, Fort Douglas, UT.

VAN METER, W.G. and KARCZMAN, A.G. 1968. Prophylactic and Antidotal Treatment of Sarin Poisoning with Drugs Given Singly and in Combination. Arch. Internat. Pharmacodyn. Therap. 172:62. In: Residue Reviews. Volume 46. (1973). The Problem of Residues in Meat of Edible Domestic Animals After Application or Intake of Organophosphate Esters. Springer-Verlag, New York. pg. 194-195.

SULFUR MUSTARD[1/]

Summary

Sulfur mustard (mustard gas) is a highly toxic compound formerly manufactured as a chemical warfare agent. It is a highly toxic vesicant (blistering agent). Sulfur mustard is toxic via all modes of exposure and has been shown to be mutagenic, teratogenic and carcinogenic in animals.

CAS Number: 505-60-2

Chemical Formula: $(ClCH_2CH_2)_2S$

IUPAC Name: 2,2-Dichlorodiethyl sulfide

Important Synonyms and Trade Names: Mustard gas; sulfur mustard

Chemical and Physical Properties

Molecular Weight: 159.1 (Sax 1979)

Boiling Point: 228°C (Sax 1979)

Melting Point: 13-14°C (Merck 1983)

Specific Gravity: 1.27 (Merck 1983)

1/ Compiled From: United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL), 1985. Physical, Chemical, and Toxicological Data Summaries for 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

Also: Department of the Army (DA). 1986. Draft Occupational Health Guidelines for the Evaluation and Control of Occupational Exposure to Agent Mustard. DA Pamphlet No. 40-XX. Headquarters, Department of the Army, Washington, D.C.

Solubility in Water: 800 mg/liter (USEPA 1985)
680 mg/liter (IARC 1975)

Solubility in Organics: Soluble in most organic solvents (Merck 1983)

Log Octanol/Water Partition Coefficient (K_{ow}): 1.37 (Lyman et al. 1982) Fragment Method

Soil/Water Partition Coefficient (K_{oc}):

132.5	Kenaga and Goring (1980) (Log K_{ow}) = 1.37)
115	Lyman et al. (1982) Eqn 4-5 (S = 740)
33.7	Lyman and Loreti (1986) Eqn I (Log K_{ow} = 1.37)
27.5	Lyman and Loreti (1986) Eqn II (Log K_{ow} = 1.37)
28.6	Lyman and Loreti (1986) Eqn III (Log K_{ow} = 1.37)
60.9	Kadeg et. al. (1986) (Log K_{ow} = 1.37)

Bioconcentration Factor:

6.47	Lyman et al. (1982) Eqn 5-2 (Log K_{ow} = 1.37)
7.35	Davies and Dobbs (1984) Eqn C (Log K_{ow} = 1.37)
10.1	Davies and Dobbs (1984) Eqn B (Low K_{ow} = 1.37)
15	Davies and Dobbs (1984) Eqn A (S = 740)

Vapor Pressure: 0.09 mm Hg at 30°C (Merck 1983)
0.17 mm Hg at 25°C (USEPA 1985)

Vapor Density: 5.4 (Sax 1979)

Henry's Law Constant: 2×10^{-5} atm-m^3/mole (calculated)
4.45×10^{-5} atm m^3/mole (USEPA 1985)

Transport and Fate

The vapor pressure of sulfur mustard indicates that some volatilization from environmental media will occur. Sulfur mustard will volatilize with steam (Merck 1983); therefore, this mode of transport may be enhanced in hot and humid environments. The subsequent chemical fate of airborne sulfur mustard is unknown.

In aqueous solution, sulfur mustard hydrolyzes rapidly to thiodiglycol. The half-life of sulfur mustard in the dissolved state is estimated to be 55 minutes at 10°C and 4 minutes at 25°C (Small 1984). In suspension, sulfur mustard undergoes a series of competing reactions which eventually result in breakdown to thiodiglycol, but initially proceed through the formation of several sulfonium salt species.

In soil or even under water, the persistence of sulfur mustard is reported to range from 3-30 years. The long residence time is thought to be due to the formation of a compound that may be insulated from reaction with water by a sulfonium-salt layer, or by the formation of a polymerized mustard-type compound (Small, 1984). A range of estimated soil/water partition coefficients is reported above and indicates that some sorption of sulfur mustard to soils and sediments may occur. The solubility of sulfur mustard suggests that non-hydrolyzed compound could be leached to some degree; however, the rapid rate of hydrolysis for sulfur mustard will likely preclude any environmental mobility of the unaltered compound.

No data were located on the potential for uptake of sulfur mustard by plants. A range of estimated bioconcentration factors for sulfur mustard is reported above. ASTM (1985) indicates that chemicals with bioconcentration factors less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the predicted concentration factors suggests that appreciable bioconcentration or biomagnification of sulfur mustard residues is not likely to occur.

Health Effects

Sulfur mustard (mustard gas) acts as a cytotoxic agent on all tissue surfaces, and is therefore hazardous through all routes of exposure (DA 1986). Repeated exposures are reported to result in hypersensitivity to its effects. Ocular exposure results in injuries ranging from mild conjunctivitis to corneal necrosis and

opacification. Skin absorption results initially in capillary hyperemia and dermal edema followed by vesication (blistering) (DA 1986). Inhalation of mustard gas produces damage primarily to the laryngeal and tracheobronchial mucosa. Severe inhalation exposures yield congestion of the pulmonary parenchyma, edema and atelectasis (collapse of part or all of the lung)(DA 1986). Mustard gas reacts *in vivo* with proteins and nucleic acids of the lung, liver and kidney of A/J mice (IARC 1975).

Ingestion of sulfur mustard results in necrosis and desquamation of gastrointestinal mucosa, producing diarrhea, gastrointestinal hemorrhage, nausea and vomiting. Systemic absorption results in injury to the bone marrow, lymph nodes and spleen, producing leukopenia and thrombocytopenia (DA 1986). Other systemic effects include fever, central nervous system depression, cardiac irregularities, hemoconcentration and shock.

Mustard gas has been shown to be mutagenic and carcinogenic in animals (IARC 1975). Mustard gas has induced mutations and chromosome rearrangements in *Drosophila melanogaster* (IARC 1975). It has also induced chromosome aberrations in cultured rat tumor cell lines (lymphosarcoma); and in a host-mediated assay in male BDF_1 mice it induced both chromosome aberrations and reverse mutations to asparagine independence following single subcutaneous doses of 100 mg/kg bw (IARC 1975). Mustard gas is a demonstrated carcinogen causing lung tumors in mice (the only species tested) following inhalation and intravenous exposures (IARC 1975). Injection subcutaneously produced injection site sarcomas (IARC 1975). In humans, prolonged exposure has been associated with cancer of the tongue, paranasal sinus, larynx, bronchus, lung and mediastinum (DA 1986).

From military experience and accidents, the estimated lethal concentration in humans via inhalation exposure is 50 mg/m^3 for 30 minutes, and 50 mg/m^3 for 200 minutes by dermal exposure (Rosenblatt et al. 1975). The acute intravenous LD_{50} value in mice is 8.6 mg/kg (Rosenblatt et al. 1975). The subcutaneous LD_{50} in rats is 2 mg/kg.

Toxicity to Wildlife and Domestic Animals

Very little data was available in the literature reviewed on the toxicity of sulfur mustard to wild or domestic animals. The acute intravenous LD_{50} value in dogs is 0.2 mg/kg (Rosenblatt et al. 1975). The acute dermal LD_{50} value in dogs is 20 mg/kg. The subcutaneous and dermal LD_{50} values for sulfur mustard in goats are 40 mg/kg and 50 mg/kg, respectively (Rosenblatt et al. 1975). The dermal LD_{50} for guinea pigs is 20 mg/kg. In rabbits, the dermal and intravenous LD_{50} values are 100 mg/kg and 1.1 mg/kg, respectively.

No data were located on the toxicity of sulfur mustard to avian or aquatic species.

Regulations and Standards

The U.S. Department of the Army suggests a "Control Limit for the General Public" (CLGP) of 0.0001 mg/m^3 when the maximum averaging time for ambient concentrations is 72 hours (USAMBRDL 1985).

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

For sulfur mustard, the D_T value should appropriately be based on cancer potency data when available. Because carcinogenicity data for sulfur mustard have not been evaluated by EPA using the linearized multi-stage model, no cancer potency slope is available for this compound. Therefore, the D_T value has instead been based on non-carcinogenic health effects data (recognizing the limitations).

The D_T Value for sulfur mustard is based on a standard known as a Control Limit for the General Public (CLGP) proposed by McNamara et al., 1975, in a special report on mustard levels in the environment and their toxicological implications. A control limit is "the maximum average airborne concentration (mg/m^3) of a substance to which it is believed that essentially all members of a specific population can be exposed for a specific period without adverse effect." The Control Limits of the General Population were proposed by McNamara et al. (1975) based on the evidence that exposure to a concentration of 0.001 mg/m^3, 24 hours/day or 0.003 mg/m^3, 8 hours/day (C_t = 1.4 mg min/m^3 per day), 5 days/week for 1 year did not produce detectable damage (systemic, local, pathological, mutagenic, teratogenic, or carcinogenic) in a variety of animal species including mice, rats, guinea pigs, rabbits and dogs. Parameters monitored during the study were blood chemistry (dogs, rabbits only), body weights, pathology and carcinogenicity, sensitization (eyes, skin, respiratory) reproductive indices (live to dead ratios, number of implantation sites - rats only), and albumium/globulin ratios (dogs, rabbits only).

Derivation of the D_T value from the CLGP standard is accomplished by utilizing an equation developed by Stokinger and Woodward (1958). The equation allows the computation of an Acceptable Daily Intake for oral exposure (ADI or D_T) from a respiratory intake concentration. An Uncertainty Factor of 1,000 is employed to address interspecies variability and intraspecies variability (sensitive subgroups) (10). An extra margin of safety (10) has been added to address the carcinogenicity of sulfur mustard as no carcinogenic potency has been determined for this chemical. Derivation of the D_T value for sulfur mustard utilizing the Stokinger and Woodward equation is as follows:

$$D_T = \frac{TLV \times BR \times d \times A_A}{BW \times A_o \times UF}$$

Where: TLV = Concentration in air (mg/m^3)
d = Days exposed (5 days/7 days)
A_A = Efficiency of absorption from air (100 percent assumed)

A_o = Efficiency of absorption from oral exposure (100 percent assumed)

UF = Uncertainty Factor

BR = Breathing Rate (m^3/day)

BW = Reference Human Body Weight (70 kg)

D_T = Contaminant Intake Rate (mg/kg/day)

$$D_T = \frac{0.003 \text{ mg/m}^3 \times 20 \text{ m}^3\text{/day} \times 5 \text{ days/7 days} \times 1}{1 \times 1{,}000 \times 70 \text{ kg}}$$

$$= 6.12 \times 10^{-7} \text{ mg/kg/day}$$

REFERENCES

ASTM. 1985. Standard Practice for conducting bioconcentration tests with fishes and saltwater bivalve mollusca. Designation E 1022-84, pages 590-62. In: 1985 Annual Book of ASTM Standards Volume 11.04. American Society for Testing and Materials, Philadelphia, Pennsylvania.

DAVIES, R.P. and A.J. DOBBS. 1984. The prediction of bioconcentration in fish. Water Res. 18(10):1253-1262.

DEPARTMENT OF THE ARMY (DA). 1986. Draft Occupational Health Guidelines for the Evaluation and Control of Occupational Exposure to Agent Mustard. DA Pamphlet No. 40-XX. Headquarters, Department of the Army, Washington, D.C.

KENAGA, E.E. and GORING, C.A.I. 1980. Relationship Between Water Solubility, Soil Sorption, Octanol-Water Partitioning and Concentration of Chemicals in Biota. In: Aquatic Toxicology, ASTM STP 707. J.G. Eaton, P.R. Parrish, and A.C. Hendricks (Eds.). American Society for Testing and Materials, pp. 78-115.

IARC (INTERNATIONAL AGENCY FOR RESEARCH ON CANCER). 1975. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man. Some aziridines, N-, S-, and O-mustards and selenium. Volume 9. IARC. Lyon.

LYMAN, W.J., REEHL, W.F., and ROSENBLATT, D.H. 1982. Handbook of Chemical Property Estimation Methods: Environmental Behavior of Organic Compounds. McGraw-Hill Book, Co., New York, NY.

LYMAN, W.J., LORETI, C.P. 1986. Prediction of Soil and Sediment Sorption for Organic Compounds (Comment Final Draft). U.S. Environmental Protection Agency, Monitoring and Data Support Division, Office of Water Regulations and Standards. Washington D.C.

McNAMARA, B.P. OWENS, M.K., CRISTENSEN, M.K., and FORD, D.F. et al. 1975. Toxicological Basis for Controlling Levels of Mustard in the Environment. Edgewood Arsenal Special Publication EB-SP-74030. Biomedical Laboratory, Edgewood Arsenal, Aberdeen Proving Ground, MD.

ROSENBLATT, D.H., T.A. MILLER, J.C. DACRE, I. MUUL and D.R. COGLEY. 1975. Problem definition studies on potential environmental pollutants. II. Physical, chemical, toxicological, and biological properties of 16 substances. Technical Report 7509. U.S. Army Medical Bioengineering Research and Development Laboratory, Fort Detrick, Frederick, MD.

SAX, I.N. 1979. Dangerous Properties of Industrial Materials, Fifth Edition. Van Nostrand Reinhold Company, New York.

SMALL, M.J. 1984. Compounds Formed From the Chemical Decontamination of HD, GB, and VX and Their Environmental Fate. Technical Report 8304. United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL). Fort Detrick, Frederick, MD. NTIS No. AD-A149515.

STOKINGER, M.E. AND WOODWARD, A.L. 1958. Toxicological Methods for Establishing Drinking Water Standards. J. Am. Water Works Assoc., 50:517.

THE MERCK INDEX. 1983. An Encyclopedia of Chemicals, Drugs and Biologicals. Tenth ed. Windholz, M., Budavan, S., Blumetti, R.F. and Otterbein, E.S. (eds.). Merck and Company, Inc., Rahway, New Jersey.

UNITED STATES ARMY MEDICAL BIOENGINEERING RESEARCH AND DEVELOPMENT LABORATORY (USAMBRDL). 1985. Physical, Chemical, and Toxicological Data Summaries of 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1985. Draft Superfund Public Health Evaluation Manual. Prepared by: ICF Incorporated, Washington D.C. USEPA Office of Solid Waste and Emergency Response, Washington D.C. EPA Contract No. 68-01-7090.

SUPONA[1/]

Summary

Supona is a member of the organophosphorus class of pesticides. Its primary mode of toxicity is through inhibition of the enzyme acetylcholinesterase (ChE) in mammalian systems. Effects on reproductive parameters in exposed rats have been observed. Chronic exposures have resulted in significant ChE depression in exposed animals.

CAS Number: 470-90-6

Chemical Formula: $C_{12}H_{14}PO_4Cl_3$

IUPAC Name: 2-Chloro-1-(2,4-dichlorophenyl)vinyl diethyl phosphate

Important Synonyms and Trade Names: Chlorofenvinophos; Supona

Chemical and Physical Properties

Molecular Weight: 360 (Merck 1983)

Melting Point: -19 to -23°C (TBD Peer Review Committee 1984)

Specific Gravity: 1.36 at 16°C (TBD Peer Review Committee 1984)

Solubility in Water: 145 mg/liter at 23°C (Merck 1983)
110 mg/liter at 20°C (Berg 1982)

1/ Compiled from: United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL), 1985. Physical, Chemical, and Toxicological Data Summaries for 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

Solubility in Organics: Miscible with acetone, ethanol and propylene glycol

Log Octanol/Water Partition Coefficient (K_{ow}): 3.11 (Briggs 1981)

Soil/Water Partition Coefficient (K_{oc}):

329; 283	Lyman et al. (1982) Eqn 4-5 (S = 110; 145)
1,170	Lyman et al. (1982) Eqn 4-8 (log K_{ow} = 3.11)
763	Lyman and Loreti (1986) Eqn I (log K_{ow} = 3.11)
778	Lyman and Loreti (1986) Eqn II (log K_{ow} = 3.11)
777	Lyman and Loreti (1986) Eqn III (log K_{ow} = 3.11)
1,080	Kadeg et al. (1986) (log K_{ow} = 3.11)

Bioconcentration Factor:

136	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 3.11)
111	Davies and Dobbs (1984) Eqn B (log K_{ow} = 3.11)
65	Davies and Dobbs (1984) Eqn C (log K_{ow} = 3.11)
40	Davies and Dobbs (1984) Eqn A (S = 130)

Vapor Pressure: 7.5×10^{-6} mm Hg at 25°C (Merck 1983)
1.7×10^{-7} mm Hg at 25°C (Edward 1973)
4×10^{-6} mm Hg at 20°C (TBD Peer Review Committee 1984)

Henry's Law Constant: 3.8×10^{-9} atm-m^3/mole (calculated)
7.3×10^{-10} atm-m^3/mole (calculated)

Transport and Fate

The low vapor pressure for supona suggests that losses through volatilization will not be a major transport process. Hydrolysis of supona occurs, but only very slowly. At a temperature of 38°C and a pH of 1.1, the half-life estimate for supona is >700 hours; while at a pH of 9.1, the half-life estimate is 400 hours (TBD Peer Review Committee 1984).

In soil, (type unspecified), TBD (1984) reports an expected loss of 50 percent in a "few weeks". Following application of supona to a sandy loam soil, 20-30 percent of the chemical remained (TBD 1984). Similar

estimates are cited in Menzie (1969, 1980). In soils treated with supona and stored for four months at 22°C, the reported degradation products were desmethyl chlorofenvinophos (Menzie 1969). A range of estimated soil/water partition coefficients (K_{OC}) is reported above and indicates that sorption of supona to soils/sediments and dissolved organic material will occur. The combined water solubility and moderate organic partitioning data for supona suggest that this compound will exhibit some degree of environmental mobility.

Uptake of supona in carrots (~0.4 ppm) was observed 50 days following soil application of 5.6 kg/ha (Edward, 1973).

A range of estimated bioconcentration factors (BCFs) for supona is also reported above. ASTM (1985) indicates that chemicals with bioconcentration factors less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the concentration factors suggests that appreciable bioconcentration or biomagnification of supona residues is not likely to occur.

Health Effects

In humans, inhibition of plasma ChE has been demonstrated following oral and dermal exposures to supona. A volunteer given a single oral dose of 1 mg/kg supona exhibited temporary glycosuria (Shell Chemical Company 1967). Erythrocyte ChE was depressed 44 percent after six hours. Twenty-six days following the initial exposure, plasma ChE of the volunteer was inhibited by 41 percent. Erythrocyte ChE recovered to within 94 percent of the pre-expsoure level after 54 days, while plasma ChE returned to 100 percent of initial levels during the same period.

Plasma ChE in male and female rats was significantly depressed at all levels after one week following consumption of supona at concentrations of 0, 10, 30, 100, or 300 ppm for up to 103 weeks (Shell Chemical Company 1967). Cholinesterase depression remained constant except in males at 10 ppm which exhibited normal levels during the

second year. During the first three months of exposure, erythrocyte ChE was inhibited only in the 30 ppm dose group. Thereafter, depression was observed at all levels but recovered in males during the second year of exposure. Females in the two high dose groups exhibited a tendency for lesser weight gains. Male and female dogs were fed supona for for two years at concentrations of 0, 30, 200, or 1,000 ppm (0, 0.75, 5 or 25 mg/kg/day). Significant depression of plasma ChE activity occurred during the first nine months of exposure at all levels (Shell Chemical Company 1967). Levels of ChE activity returned to within control levels thereafter. Depression of erythrocyte ChE occurred at 1,000 ppm consistently for 12 weeks and was sporadic thereafter (Shell Chemical Company 1967). A subchronic oral toxicity study in beagle dogs utilizing dose levels of 0, 0.5, 1, or 3 ppm (0, 0.0125, 0.025, or 0.075 mg/kg/day) resulted in a No-Observed-Effect-Level (NOEL) of 3 ppm (Shell Chemical Company 1967).

In a three generation reproduction study, albino rats fed concentrations of supona at 0, 30, 100, or 300 ppm (0, 0.75, 2.5, or 7.5 mg/kg/day) exhibited effects on certain reproductive parameters (Shell Chemical Company 1967). At the two high dose levels, interference with gestation (and possibly lactation) occurred. Effects on weanling survival rates were also observed. Only nine of 20 second generation females at 30 ppm cast litters compared with 18 of 20 control females. Twenty females exposed to 30 ppm supona in the second and third generations also experienced a reduction in the number of litters cast (six of twenty) compared with controls (14 of 20). Data on mutagenicity and carcinogenicity of supona were not located in available literature.

Acute oral lethality values (LD_{50}) for rats and mice fed supona ranged from 10 to 39 mg/kg (rats) and from 117 to 200 mg/kg for mice (NIOSH 1983, TBD Peer Review Committee 1984).

Toxicity to Wildlife and Domestic Animals

No data was located on the toxicity of supona to aquatic organisms. The acute oral toxicities (LD_{50}) of supona to rabbits and guinea pigs are 500 mg/kg and 125 mg/kg, respectively (NIOSH 1983). In goats and sheep the oral LD_{50} is 71.25 mg/kg while in cattle the oral LD_{50} is 20 mg/kg.

Acute toxicity data are available for avian species such as the mallard duck (Anas platyrhyncos) the bobwhite quail (Colinus virginianus) and the ring-necked pheasant (Phasianus colchicus). The acute oral toxicity values (LD_{50}) for these species are (respectively) 85 mg/kg, 80-160 mg/kg and 63.5 mg/kg (Hudson et al. 1984).

Regulations and Standards

None located.

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

For supona, the D_T value is based on a subchronic (120 day) oral feeding study in beagle dogs (Shell Chemical Company 1967). Groups of dogs were fed dietary concentrations of 0.5, 1.0 and 3.0 ppm supona (0.025, 0.05, and 0.15 mg/kg/day). No effects on cholinesterases were observed. Liver function tests were normal at the conclusion of the feeding period and autopsy failed to show any gross or histological abnormalties. The No-Observed-Effect-Level (NOEL) was identified as 3 ppm (0.15 mg/kg/day) (Shell Chemical Company 1967). An Uncertainty Factor (UF) of 1,000 is included in the derivation of the D_T value to address extrapolation of the results to humans (10), intraspecies

variability (sensitive subgroups) (10), and to account for using a subchronic rather than a chronic exposure duration (10). Derivation of the D_T for supona is as follows:

$$D_T = \frac{\text{NOEL}}{\text{UF}} \text{ (mg/kg/day)}$$

$$= \frac{0.15}{1{,}000}$$

$$= 0.00015 \text{ mg/kg/day}$$

References

ASTM. 1985. Standard Practice for conducting bioconcentration tests with fishes and saltwater bivalve mollusca. Designation E 1022-84, pages 590-62. In: 1985 Annual Book of ASTM Standards Volume 11.04. American Society for Testing and Materials, Philadelphia, Pennsylvania.

BERG, G.L. (Editor). 1982. Farmers Chemical Handbook. Meister Publishing Co., Willoughby, OH.

BRIGGS, C.L. 1981. Theoretical and experimental relationships between soil adsorption, octanol-water partition coefficients, water solubilities, bioconcentration factors, and the parachor. J. Agric. Food Chem., 29:1050-1059.

DAVIES, R.P. and A.J. DOBBS. 1984. The prediction of bioconcentration in fish. Water Res. 18(10):1253-1262.

EDWARD, C.A. (Editor). 1973. Environmental Pollution by Pesticides. Plenum Press, New York, NY.

HUDSON, R.H., TUCKER, R.K. AND HAEGALE, M.A. 1984. Handbook of Toxicity of Pesticides to Wildlife. Second Edition. United States Department of the Interior Fish and Wildlife Service. Resource Publication 153. Washington, D.C. 1984.

KADEG, R.D., PAVLOU, S.P., DUXBURY, A.S. 1986. Elaboration of Sediment Normalization Theory for Non Polar Hydrophobic Organic Chemicals. U.S. Environmental Protection Agency, Criteria and Standards Division, Washington D.C.

LYMAN, W.J., LORETI, C.P. 1986. Prediction of Soil and Sediment Sorption for Organic Compounds (Comment Final Draft). U.S. Environmental Protection Agency, Monitoring and Data Support Division, Office of Water Regulations and Standards. Washington D.C.

LYMAN, W.J., W.F. REEHL AND D.H. ROSENBLATT. 1982. Handbook of Chemical Property Estimation Methods: Environmental Behavior of Organic Compounds. McGraw-Hill Book Co., New York, NY.

MENZIE, C.M. 1980. Metabolism of Pesticides, Update III. U.S. Department of the Interior, Fish and Wildlife Service. Special Scientific Report No. 232. Washington, D.C.

MENZIE, C.M. 1969. Metabolism of Pesticides. U.S. Department of the Interior, Fish and Wildlife Service. Special Scientific Report No. 127. Washington, D.C.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH). 1983. Registry of Toxic Effect of Chemical Substances. Data Base. Washington D.C. October 1983.

SHELL CHEMICAL COMPANY. 1967. Summary of the Toxicology of Supona. [Proprietary Information.] Technical Report No. M-537-67, No. 3.

TBD PEER REVIEW COMMITTEE. 1984. Toxicology Data Bank, National Library of Medicine and National Institutes of Health. Department of Health and Human Services, Washington, D.C. (Computerized Data Base).

THE MERCK INDEX. 1983. An Encyclopedia of Chemicals, Drugs and Biologicals. Tenth ed. Windholz, M., Budavan, S., Blumetti, R.F. and Otterbein, E.S. (eds.). Merck and Company, Inc., Rahway, New Jersey.

TETRACHLOROETHYLENE[1/]

Summary

Tetrachloroethylene (PCE) induced liver tumors following oral administration to mice. Tetrachloroethylene has also been shown to be mutagenic in bacterial systems. Reproductive toxicity was observed in pregnant rats and mice following exposure to high concentrations of tetrachloro-
ethylene. Animals exposed via inhalation exhibited liver, kidney, and central nervous system damage. In humans, central nervous system depression and liver toxicity are also the principal effects exhibited following tetrachloroethylene exposure.

CAS Number: 127-18-4

Chemical Formula: C_2Cl_4

IUPAC Name: Tetrachloroethene

Important Synonyms and Trade Names: Perchloroethylene, PCE

Chemical and Physical Properties

Molecular Weight: 165.83

Boiling Point: 121°C

Melting Point: -22.7°C

1/ Compiled from: U.S. Environmental Protection Agency, Office of Waste Program Enforcement. September 1985. Chemical, physical, and biological properties of compounds present at hazardous waste sites. A Final Report Prepared by Clement Associates, Inc., Arlington, Virginia.

Also: United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL). 1985. Physical, Chemical, and Toxicological Data Summaries of 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

Specific Gravity: 1.63

Solubility in Water: 150 - 200 mg/liter at 20°C

Solubility in Organics: Soluble in alcohol, ether, and benzene

Log Octanol/Water Partition Coefficient (K_{ow}): 2.60 (Hansch and Leo 1979)
2.53 (Veith et al. 1983)

Soil/Water Partition Coefficient (K_{oc}):

360	Chiou et al. (1979) (experimental)
546; 619	Lyman et al. (1982) Eqn 4-8 (log K_{ow} = 2.5, 2.6)
277 - 143	Lyman et al. (1982) Eqn 4-5 (S = 150 - 500)
280	Lyman and Loreti (1986) Eqn I (log K_{ow} = 2.55)
265	Lyman and Loreti (1986) Eqn II (log K_{ow} = 2.55)
269	Lyman and Loreti (1986) Eqn III (log K_{ow} = 2.55)
427	Kadeg et al. (1986) (log K_{ow} = 2.55)

Bioconcentration Factor:

49	Davies and Dobbs Table 2 (experimental)
38-19	Davies and Dobbs (1984) Eqn A (S = 140-500)
30.6	ECAO 1980
55.7	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 2.6)
49.3	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 2.53)
26.9	Davies and Dobbs (1984) Eqn C (log K_{ow} = 2.55)
51.3	Davies and Dobbs (1984) Eqn B (log K_{ow} = 2.55)
51.1	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 2.55)

Vapor Pressure: 14 mm Hg at 20°C

Henry's Law Constant: 1.4×10^{-2} atm-m^3/mole (calculated)
2.59×10^{-2} atm-m^3/mole (USEPA 1985)

Transport and Fate

Tetrachloroethylene volatilizes rapidly into the atmosphere where it reacts with hydroxyl radicals to produce HCl, CO, CO_2 and carboxylic acid. This is probably the most important transport and

fate process for tetrachloroethylene in the environment. The half-life of PCE in air is approximately 47 days (USEPA 1984). The half-life of PCE in water may range from 1-30 days (USEPA 1985).

A range of experimental and estimated soil-water partition coefficients (K_{oc}) is reported above and indicates that sorption of tetrachloroethylene to soils/sediments and dissolved organic material will occur. Pavlou (1980) estimates that sorption of volatile organic compounds will range from low to moderate. The combined water solubility and organic partitioning data indicate that tetrachloroethylene will exhibit some degree of environmental mobility. It is uncertain if organically bound tetrachloroethylene can be efficiently degraded by microorganisms.

A range of experimental and estimated bioconcentration factors (BCFs) for tetrachloroethylene is also reported above. ASTM (1985) indicates that chemicals with bioconcentration factors less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the concentration factors suggest that appreciable bioconcentration or biomagnification of tetrachloroethylene residues is not likely to occur.

Health Effects

Health effects in humans following chronic exposure to tetrachloroethylene include respiratory tract irritation, nausea, headache, sleeplessness, abdominal pains, constipation, liver cirrhosis, hepatitis, and nephritis (USEPA 1984). However, central nervous system depression and liver toxicity are the principal systemic effects exhibited following tetrachloroethylene exposure (acute, chronic). Blair et al. (1979) observed an excess of lung, cervical, and skin cancers and slight increases in leukemia and liver cancer in a study of deceased laundry and dry-cleaning workers with known exposures to PCE, carbon tetrachloride, and trichloroethylene.

Tetrachloroethylene was not mutagenic in several Salmonella typhimurium strains either with or without metabolic activation (National Toxicology Program 1986). It was not mutgenic in mouse lymphoma cells with or without metabolic activation and did not induce sex-linked recessive lethal mutations in Drosophila melanogaster (National Toxicology Program 1986). Tetrachloroethylene did not induce sister chromatid exchanges or chromosomal aberrations in Chinese hamster ovary cells with or without metabolic activation. In male and female mice, tetrachloroethylene was found to produce liver cancer when orally administered by gavage (NCI 1977). The National Toxicology Program (NTP) recently completed a chronic (103 week) inhalation study with PCE in rats and mice (NTP 1986). The exposure concentrations were 0, 200, or 400 ppm for rats and 0, 100, or 200 ppm for mice. Survival of male rats was affected at the high dose and survival of male mice was affected at both doses. Survival of female mice was reduced at 200 ppm. Both concentrations of PCE were associated with leukemia in male and female rats. PCE caused renal tubular cell hyperplasia in male rats, renal tubular cell adenomas or adenocarcinomas in male rats (not statistically significant), and renal tubular cell karyomegaly in male and female rats. One low dose male rat had a kidney lipoma and another had a nephroblastoma. In male and female mice, PCE caused increased incidences of hepatocellular neoplasms. High dose males had increased incidences of hepatocellular adenomas while an increased incidence of hepatocellular carcinomas occurred at both concentrations in males and females. As was observed in rats, PCE produced renal tabular cell karyomegaly. No neoplastic changes were observed in the respiratory tracts of either species; however, an increased incidence of squamous metaplasia was observed in the nasal cavities of dosed male rats. Teterachloroethylene has been classified according to EPA's Guidelines for Carcinogenic Risk Assessment in EPA's Group B2 (probable human carcinogen) based on sufficient evidence in animals and inadequate evidence in humans (USEPA 1986a).

Delayed ossification of skull bones and sternebrae were reported in the offspring of pregnant mice exposed via inhalation to concentrations of 2,000 mg/m^3 tetrachloroethylene. The exposure duration was

7 hours/day and spanned days 6-15 of gestation. In another study, increased fetal resorptions were observed following exposure of pregnant rats to tetrachloroethylene. Renal toxicity and hepatotoxicity were exhibited by rats following chronic inhalation exposure at levels of 1,356 mg/m^3 tetrachloroethylene. During the first 2 weeks of a subchronic inhalation study, exposure to concentrations of 1,622 ppm (10,867 mg/m^3) of tetrachloroethylene produced signs of central nervous system depression and cholinergic stimulation in rabbits, monkeys, rats, and guinea pigs.

Toxicity to Wildlife and Domestic Animals

Tetrachloroethylene is the most toxic of the chloroethylenes to aquatic organisms. Limited acute toxicity data are available for PCE; however, these data appear to indicate that the LC_{50} values for saltwater and freshwater species are similar--approximately 10,000 µg/liter. The trout was the most sensitive species evaluated (LC_{50} = 4,800 µg/liter). Chronic values were 840 and 450 µg/liter for freshwater and saltwater species, respectively. An acute-chronic ratio of 19 has been computed for tetrachloroethylene.

No information on the toxicity of tetrachloroethylene to terrestrial wildlife or domestic animals was available in the literature reviewed.

Regulations and Standards

Ambient Water Quality Criteria (USEPA 1986b):

The available data are not adequate for establishing criteria. However, EPA does report the lowest values known to be toxic to aquatic organisms.

Aquatic Life (Freshwater)

Acute toxicity: 5,280 µg/liter
Chronic toxicity: 840 µg/liter

Aquatic Life (Saltwater)

Acute toxicity: 10,200 µg/liter
Chronic toxicity: 450 µg/liter

Human Health

Due to the carcinogenicity of tetrachloroethylene the ambient water criterion is set at zero. However, estimates of the carcinogenic risks associated with lifetime exposure from ingestion of contaminated water and contaminated aquatic organisms are:

Risk	Concentration
10^{-5}	8.0 µg/liter
10^{-6}	0.8 µg/liter
10^{-7}	0.08 µg/liter

CAG Potency Slope for oral exposure (USEPA 1986a): 5.1×10^{-2} $(mg/kg/day)^{-1}$

CAG Potency Slope for inhalation exposure (USEPA 1986a): 1.7×10^{-3} $(mg/kg/day)^{-1}$

NIOSH Recommended Standards (air): TWA[1/] = 335 mg/m^3
Ceiling Level = 670 mg/m^3 (15 min.)

OSHA Standards (air): TWA = 670 mg/m^3
Ceiling Level = 1,340 mg/m^3
Peak Level = 2,010 mg/m^3 (5 min every 3 hr.)

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or

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1/ Time Weighted Average

should not pose a risk of cancer occurrence greater than a predetermined risk level.

For carcinogens such as tetrachloroethylene the D_T value is based on the USEPA Cancer Assessment Group's cancer potency slopes. The cancer potency slopes have been estimated for oral exposure routes and for inhalation exposure for tetrachloroethylene. The slopes are intended to be a plausible upper bound of the potency of a carcinogen in inducing cancer at low doses. Calculation of a D_T using a cancer potency slope requires selection of an acceptable cancer risk level. A range of risk levels from 10^{-4} to 10^{-7} is considered for all carcinogens, therefore a range of D_T values is presented. Derivation of the D_T values for tetrachloroethylene is as follows:

$$D_T = \frac{\text{Risk Level}}{\text{Potency Slope}^{\text{(mg/kg/day)}^{-1}}}$$

$$= \frac{1 \times 10^{-4}}{5.1 \times 10^{-2}}$$

$$= 1.9 \times 10^{-3} \text{ mg/kg/day}$$

The range of D_T values for tetrachloroethylene is presented below:

Risk Level	D_T Oral Exposure (mg/kg/day)	D_T Inhalation Exposure (mg/kg/day)
10^{-4}	1.9×10^{-3}	5.9×10^{-2}
10^{-5}	1.9×10^{-4}	5.9×10^{-3}
10^{-6}	1.9×10^{-5}	5.9×10^{-4}
10^{-7}	1.9×10^{-6}	5.9×10^{-5}

REFERENCES

ASTM. 1985. Standard Practice for conducting bioconcentration tests with fishes and saltwater bivalve mollusca. Designation E 1022-84, pages 590-62. In: 1985 Annual Book of ASTM Standards Volume 11.04. American Society for Testing and Materials, Philadelphia, Pennsylvania.

BLAIR, A., DEGOUFLE, P., AND GRAUMAN, D. 1979. Causes of death among laundry and dry cleaning workers. Am. J. Publ. Health. 69:508-511 (Cited in USEPA 1984).

CHIOU, C.T., J.L. Peters and V.H. Freed. 1979. A physical concept of soil-water equilibria for nonionic organic compounds. Science, 206:831-832.

DAVIES, R.P. and DOBBS, A.J. 1984. The prediction of bioconcentration in fish. Water Res. 18(10): 1253-1262.

ECAO 1980. See USEPA 1980.

HANSCH, C. and LEO, A. 1979. Substituent constants for correlation analysis in chemistry and biology. John Wiley and Sons, New York, NY.

LYMAN, W.J., LORETI, C.P. 1986. Prediction of Soil and Sediment Sorption for Organic Compounds (Comment Final Draft). U.S. Environmental Protection Agency, Monitoring and Data Support Division, Office of Water Regulations and Standards. Washington D.C.

LYMAN, W.J., W.F. REEHL and D.H. ROSENBLATT. 1982. Handbook of chemical property estimation methods: environmental behavior of organic compounds. McGraw-Hill Book, Co., New York, NY.

KADEG, R.D., PAVLOU, S.P., DUXBURY, A.S. 1986. Elaboration of Sediment Normalization Theory for Non Polar Hydrophobic Organic Chemicals. U.S. Environmental Protection Agency, Criteria and Standards Division, Washington D.C.

NATIONAL ACADEMY OF SCIENCE (NAS). 1977. Drinking Water and Health. Safe Drinking Water Committee, Washington, D.C.

NATIONAL CANCER INSTITUTE (NCI). 1977. Bioassay of Tetrachloroethylene for Possible Carcinogenicity. NCI Carcinogenesis Technical Report Series No. 13, Washington, D.C. DHEW Publication NO. (NIN) 77-813.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH). 1983. Registry of Toxic Effects of Chemical Substances. Data Base. Washington D.C. October 1983.

NATIONAL TOXICOLOGY PROGRAM (NTP). 1986. Toxicology and Carcinogenesis Studies of Tetrachloroethylene (Perchloroethylene) In F394/N Rats and B6C3F$_1$ Mice (Inhalation Studies). U.S. Department of Health and Human Services, Public Health Service. NTP Technical Report No. 311.

PAVLOU, S.P. 1980. Thermodynamic Aspects of Equilibrium Sorption of Persistent Organic Molecules at the Sediment-Seawater Interface: A Framework For Predicting Distributions in the Aquatic Environment. IN: Contaminants and Sediments. Volume 2. Baker, R.A. (Editor). Science Publishers, Inc. Ann Arbor, MI.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1979. Health Assessment Document for Tetrachloroethylene (Perchloroethylene). External Review Draft No. 1, April 1979.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1979. Water-Related Environmental Fate of 129 Priority Pollutants. Washington D.C. December 1979. EPA 440/4-79-029.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1980. Ambient Water Quality Criteria for Tetrachloroethylene. Office of Water Regulations and Standards, Criteria and Standards Division, Washington D.C. October 1980. EPA 440/5-80-073.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1984. Health Effects Assessment for Tetrachloroethylene. Final Draft. Environmental Criteria and Assessment Office, Cincinnati, Ohio. September 1984. ECAO-CIN-H009.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1985. Draft Superfund Public Health Evaluation Manual. Prepared by: ICF Incorporated, Washington, D.C. USEPA Office of Solid Waste and Emergency Response, Washington, D.C. EPA Contract No. 68-01-7090.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1986a. Health Assessment Document for Tetrachloroethylene and Addendum: Updated Carcinogenicity Assessment for Tetrachloroethylene. Office of Health and Environmental Assessment. Washington, D.C. April 1986. EPA 600/8-82/005FA.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1986b. Quality Criteria for Water, 1986 ("The Gold Book"). Office of Water Regulations and Standards, Washington, DC. EPA 440/5-86-001.

VEITH, G.D., D.J. CALL AND L.T. BROOKE. 1983. Structure-toxicity relationships for the fathead minnow, Pimephales promela: Narcotic industrial chemicals. Can. J. Fish. Aquat. Sci. 40:743-748.

VERSCHUEREN, K. 1977. Handbook of Environmental Data on Organic Chemicals. Van Nostrand Reinhold Co., New York. 659 pages.

WEAST, R.E., ed. 1981. Handbook of Chemistry and Physics. 62nd ed. CRC Press, Cleveland, Ohio. 2332 pages.

THIODIGLYCOL[1/]

Summary

Thiodiglycol is a highly water soluble and environmentally mobile sulfur compound. No subchronic or chronic toxicity data are currently available for thiodiglycol. Additionally, no data are available on reproductive toxicity, mutagenicity or carcinogenicity. Limited acute data are available. The oral LD_{50} in guinea pigs is 3,960 mg/kg, indicating a low acute toxicity in this species.

CAS Number: 111-48-8

Chemical Formula: $C_4H_{10}O_2S$

IUPAC Name: 2,2'-Thiodiethanol

Important Synonyms and Trade Names: Thiodiethylene glycol; 2,2-Thiodiethanol

Chemical and Physical Properties

Molecular Weight: 122.2 (Merck 1983)

Boiling Point: 282°C (Sax 1979)

Melting Point: -16°C (Merck 1983)

Solubility in Water: Completely Soluble (Union Carbide Corp 1970)

1/ Compiled From: United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL), 1985. Physical, Chemical, and Toxicological Data Summaries for 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

Log Octanol/Water Partition Coefficient (K_{ow}): -0.77 (Small 1984)

Soil/Water Partition Coefficient (K_{oc}): Not Applicable

Bioconcentration Factor: Not Applicable

Vapor Pressure: 1.9×10^{-5} at 25°C (Small 1984)

Vapor Density: 4.21 (Sax 1979)

Henry's Law Constant: Not Applicable

Transport and Fate

The infinite solubility of thiodiglycol in water suggests that it would be readily leached from soil. The vapor pressure of thiodiglycol indicates that volatilization is not likely to be a major transport process from environmental media. Data on the stability of thiodiglycol in air, soil, and water was not located in available literature.

Little sorption of thiodiglycol to soils or sediments is expected to occur given its high solubility in water. Therefore, thiodiglycol is likely to be an environmentally mobile contaminant.

Bioconcentration data for thiodiglycol were not located in available literature. However, given its completely soluble nature and low organic partitioning behavior, bioconcentration would not be expected to occur. No data on the uptake of thiodiglycol by plants or its subsequent bioavailability was located in the available literature.

Health Effects

No data were located on the subchronic or chronic toxicity, reproductive toxicity, teratogenicity, mutagenicity or carcinogenicity of thiodiglycol in the available literature. Thiodiglycol is

classified as a skin and eye irritant (NIOSH 1986). Acute lethality data (LD_{50}) are available for rats, mice, rabbits, and guinea pigs (NIOSH 1986). In rats and mice the subcutaneous LD_{50} values are 4,000 mg/kg for both animals (NIOSH 1986). The intravenous LD_{50} in rabbits is 3,000 mg/kg. In guinea pigs the oral LD_{50} is 3,960 mg/kg.

Toxicity to Wildlife and Domestic Animals

The only available toxicity data for thiodiglycol is summarized above.

Regulations and Standards

None located.

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

For thiodiglycol, the D_T value is derived from an acute oral LD_{50} value in guinea pigs (NIOSH, 1986). The D_T value is computed as the product of the acute value and an application factor of 1×10^{-5} (Layton et al. 1986). The application factor allows the derivation of an interim acceptable long-term intake rate (D_T) based on the results of acute tests in the absence of more suitable long-term studies (i.e., chronic studies). The application factor corresponds to the cumulative percentile on a lognormal distribution of NOEL/LD_{50} ratios for various chemicals. The percentile was chosen to reduce the probability that the calculated dose rate would be above a toxic level; the 5th cumulative percentile was used by Layton et al. (1986) and was found to be equal to 10^{-3}. The application factor also includes a safety factor of 100 to address interspecies and

intraspecies variability; therefore, an interim estimate of D_T is obtained when the application factor is multiplied by the acute value. Derivation of this D_T value is as follows:

$$D_T = \text{Acute } LD_{50} \times \text{Application Factor}$$
$$= 3{,}960 \text{ mg/kg/day} \times 1 \times 10^{-5}$$
$$= 0.0396 \text{ mg/kg/day}$$

REFERENCES

LAYTON, D.W., MALLOU, B.J., ROSENBLATT, D.H. and SMALL, M.J. 1986. Deriving Allowable Daily Intakes For Systemic Toxicants Lacking Chronic Toxicity Data. Regulatory Toxicology and Pharmacology. In Press.

LYMAN, W.J., REEHL, W.F., and ROSENBLATT, D.H. 1982. Handbook of Chemical Property Estimation Methods: Environmental Behavior of Organic Compounds. McGraw-Hill Book Co., New York.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH). 1986. Registry of Toxic Effect of Chemical Substances. Data Base. Washington D.C.

THE MERCK INDEX. 1983. An Encyclopedia of Chemicals, Drugs and Biologicals. Tenth ed. Windholz, M., Budavan, S., Blumetti, R.F. and Otterbein, E.S. (eds.). Merck and Company, Inc., Rahway, New Jersey.

UNION CARBIDE CORPORATION. 1970. Product Information Sheet F-42524-Kromfax™ Thiodiglycol. Union Carbide Corporation, New York, NY.

SAX, I.N. 1979. Dangerous Properties of Industrial Materials, Fifth Edition. Van Nostrand Reinhold Company, New York.

SMALL, M.J. 1984. Compounds Formed From the Chemical Decontamination of HD, GB, and VX and Their Environmental Fate. Technical Report 8304. United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL). Fort Detrick, Frederick, MD. NTIS No. AD-A149515.

TOLUENE[1/]

Summary

Toluene has been shown to be embryotoxic in experimental animals. An increased incidence of cleft palate was observed in the offspring of exposed mice. Chronic inhalation exposure to high levels of toluene caused cerebellar degeneration and an irreversible encephalopathy in animals. In humans, acute exposure yields central nervous system depression and narcosis.

CAS Number: 108-88-3

Chemical Formula: $C_6H_5CH_3$

IUPAC Name: Methylbenzene

Important Synonyms and Trade Names: Toluol, phenylmethane

Chemical and Physical Properties

Molecular Weight: 92.13

Boiling Point: 110°C

Melting Point: -95°C

1/ Compiled from: U.S. Environmental Protection Agency, Office of Waste Program Enforcement. September 1985. Chemical, physical, and biological properties of compounds present at hazardous waste sites. A Final Report Prepared by Clement Associates, Inc., Arlington, Virginia.

Also: United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL). 1985. Physical, Chemical, and Toxicological Data Summaries of 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

Specific Gravity: 0.8669 at 20°C

Solubility in Water: 534.8 mg/liter (USEPA 1985)
515 mg/liter (Wilson et al., 1981)

Solubility in Organics: Soluble in acetone, ligroin, and carbon disulfide; miscible with alcohol, ether, benzene, chloroform, glacial acetic acid, and other organic solvents

Log Octanol/Water Partition Coefficient (K_{ow}): 2.69 (Geyer et al. 1984; Moriguchi 1975)
2.65 (Tewari et al., 1982)
2.58 (Valvani et al., 1980)

Soil/Water Partition Coefficient (K_{oc}):

139	Lyman et al. (1982) Eqn 4-5 (S = 525)
650	Lyman et al. (1982) Eqn 4-8 (log K_{ow} = 2.64)
328	Lyman and Loreti (1986) Eqn I (log K_{ow} = 2.64)
315	Lyman and Loreti (1986) Eqn II (log K_{ow} = 2.64)
319	Lyman and Loreti (1986) Eqn III (log K_{ow} = 2.64)
495	Kadeg et al. (1986) (log K_{ow} = 2.64)

Bioconcentration Factor:

59	Davies and Dobbs (1984) Eqn B (log K_{ow} = 2.65)
53.8	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 2.58)
60.8	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 2.65)
65.2	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 2.69)
18.1	Davies and Dobbs (1984) Eqn A (S = 525)
34	Davies and Dobbs (1984) Eqn C (log K_{ow} = 2.6)
29.9	Davies and Dobbs (1984) Eqn C (log K_{ow} = 2.64)
58.1	Davies and Dobbs (1984) Eqn B (log K_{ow} = 2.64)
59.8	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 2.64)

Vapor Pressure: 28.7 mm Hg at 25°C (USEPA 1985)

Vapor Density: 3.14

Flash Point: 4.4°C

Henry's Law Constant: 6.6×10^{-3} atm-m^3/mole (calculated)
6.37×10^{-3} atm-m^3/mole (USEPA 1985)

Transport and Fate

Volatilization appears to be the major route of removal of toluene from aquatic environments and atmospheric reactions of toluene probably subordinate all other fate processes (USEPA 1979). Photooxidation is the primary atmospheric fate process for toluene, and benzaldehyde is the principal organic degradation product. Subsequent precipitation or dry deposition can deposit toluene and its oxidation products into aquatic and terrestrial systems. Direct photolytic cleavage of toluene is energetically improbable in the troposphere, and oxidation and hydrolysis are probably not important as aquatic fates.

A range of estimated soil-water partition coefficients (K_{oc}) is reported above and indicates that sorption of toluene to soils/sediments and dissolved organic material will occur. Pavlou (1980) estimates that sorption of volatile organic compounds will range from low to moderate. The combined water solubility and organic partitioning data suggest that toluene will exhibit some degree of environmental mobility. Although toluene is known to be degraded by microorganisms and can be detoxified and excreted by mammals, the available data do not allow estimation of the relative importance of biodegradation/biotransformation processes. However, Overcash et al., 1982 report that fungi and soil microorganisms are capable of using toluene as a carbon source. They also reported that less than 6.25 percent of applied toluene was retained in soil one week following application as part of a laboratory test.

A range of estimated bioconcentration factors (BCFs) for toluene is also presented above. ASTM (1985) indicates that chemicals with bioconcentration factors less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the concentration factors suggests that appreciable bioconcentration or biomagnification of toluene residues is not likely to occur

Health Effects -

There is no conclusive evidence that toluene is carcinogenic or mutagenic in animals or humans (USEPA 1980). A long-term inhalation study in rats (CITT, Unpublished 1980; 50 Federal Register 47005, Wed. Nov. 13, 1985) concluded that toluene was not carcinogenic following inhalation by rats. The National Toxicological Program is currently conducting inhalation and gavage carcinogenicity bioassays in both rats and mice. Toluene has been classified according to EPA's Guidelines for Carcinogenic Risk Assessment in EPA's Group D (not classified), based on negative results in an inhalation study and inadequate data on ingestion exposure (50 Federal Register 47005).

Oral administration of toluene at doses as low as 260 mg/kg produced a significant increase in embryonic lethality in mice (USEPA 1980). Decreased fetal weight was observed at doses as low as 434 mg/kg, and an increased incidence of cleft palate was seen at doses as low as 867 mg/kg. Other researchers, however, have reported that toluene is embryotoxic but not teratogenic in laboratory animals.

Acute exposure to toluene at concentrations of 375-1,500 mg/m^3 produces central nervous system depression and narcosis in humans (ACGIH 1980). However, even exposure to quantities sufficient to produce unconsciousness fail to produce residual organ damage. The rat oral LD_{50} value is between 5,000 and 7,000 mg/kg. The inhalation LC_{50} value in the rat varies between 33,000 and 46,000 mg/m^3 at 4 and 6.5 hours exposure, respectively. Chronic inhalation exposure to toluene at relatively high concentrations produces cerebellar degeneration and an irreversible encephalopathy in mammals. Toluene in sufficient amounts appears to have the potential to alter significantly the metabolism and resulting bioactivity of certain chemicals. For example, coadministration of toluene with benzene or styrene has been shown to suppress the metabolism of benzene or styrene in rats.

Toxicity to Wildlife and Domestic Animals

Of five freshwater species tested with toluene, the Cladoceran Daphnia magna was most resistant to acute effects (USEPA 1980). The EC_{50} and LC_{50} values for all five species range from 12,700 to 313,000 µg/liter. No chronic tests are available for freshwater species. The two freshwater algal species tested are relatively insensitive to toluene with EC_{50} values of 245,000 µg/liter or greater being reported. For saltwater species, EC_{50} and LC_{50} values range from 3,700 µg/liter for the bay shrimp to 1,050 mg/liter for the Pacific oyster. The chronic value in an embryo-larval test for the sheepshead minnow is reported to be between 3,200 and 7,700 µg/liter, and the acute-chronic ratio is between 55 and 97. In several saltwater algal species and kelp, effects occur at toluene concentrations ranging from 8,000 to greater than 433,000 µg/liter.

Regulations and Standards

Ambient Water Quality Criteria (USEPA 1986a):

The available data are not adequate for establishing criteria. However, EPA does report the lowest concentrations of toluene known to be toxic to aquatic organisms.

Aquatic Life (Freshwater)

Acute toxicity: 17,500 µg/liter
Chronic toxicity: No available data

Aquatic Life (Saltwater)

Acute toxicity: 6,300 µg/liter
Chronic toxicity: 5,000 µg/liter

Human Health

Criterion: 14.3 mg/liter

National Primary Drinking Water Standard (USEPA): 2.0 mg/liter (Proposed RMCL; 50 Federal Register 47005, Wednesday November 13, 1985).

NIOSH Recommended Standards: TWA[1/] = 375 mg/m^3
STEL[2/] = 560 mg/m^3

OSHA Standards: TWA = 750 mg/m^3
Ceiling Level = 1,120 mg/m^3

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

For toluene the D_T value is based on the same data used by EPA to compute the current Risk Reference Dose (RfD) (USEPA 1986b). The RfD is based on a chronic (24 month) inhalation study utilizing male and female rats exposed to toluene (113, 377, or 1,130 mg/m^3) 6 hours/day, 5 days/week (CIIT 1980). Clinical chemistry, hematology and urinalysis testing were conducted at 18 and 24 months. All parameters were normal at termination of the study except for a dose-related reduction in hematocrit values in females exposed to 377 or 1,130 mg/m^3. The identified No-Observed-Adverse-Effect-Level (NOAEL) from this study was 1,130 mg/m^3 (29 mg/kg/day). An Uncertainty Factor (UF) of 100 is employed to address the extrapolation of results to humans (10) and to account for intraspecies variability (sensitive subgroups) (10). Derivation of the D_T (RfD) is as follows:

$$D_T = \frac{\text{NOAEL (mg/kg/day)}}{\text{UF}}$$

$$= \frac{29}{100}$$

$$= 0.3 \text{ mg/kg/day}$$

1/ Time Weighted Average.
2/ Short-Term Effect Level.

REFERENCES

ASTM. 1985. Standard Practice for conducting bioconcentration tests with fishes and saltwater bivalve mollusca. Designation E 1022-84, pages 590-62. In: 1985 Annual Book of ASTM Standards Volume 11.04. American Society for Testing and Materials, Philadelphia, Pennsylvania.

AMERICAN CONFERENCE OF GOVERNMENTAL INDUSTRIAL HYGIENISTS (ACGIH). 1980. Documentation of the Threshold Limit Values. 4th ed. Cincinnati, Ohio. 488 pages.

CIIT. (Chemical Industry Institute of Toxicology). 1980. A twenty-four month inhalation toxicology study in Fischer-344 rats exposed to atmospheric toluene. CIIT, Research Triangle Park, NC.

DAVIES, R.P. and A.J. DOBBS. 1984. The prediction of bioconcentration in fish. Water Res. 18(10):1253-1262.

GEYER, H., POLITZKI, G., AND FREITAG, D. 1984. Prediction of exotoxicological behavior of chemicals: Relationship between n-octanol-water partition coefficient and bioaccumulation of organic chemicals by alga Chlorella. Chemosphere, 13(2): 269-284.

KADEG, R.D., PAVLOU, S.P., DUXBURY, A.S. 1986. Elaboration of Sediment Normalization Theory for Non Polar Hydrophobic Organic Chemicals. U.S. Environmental Protection Agency, Criteria and Standards Division, Washington D.C.

LYMAN, W.J., LORETI, C.P. 1986. Prediction of Soil and Sediment Sorption for Organic Compounds (Comment Final Draft). U.S. Environmental Protection Agency, Monitoring and Data Support Division, Office of Water Regulations and Standards. Washington D.C.

LYMAN, W.J., REEHL, W.F., and ROSENBLATT, D.H. 1982. Handbook of Chemical Property Estimation Methods: Environmental Behavior of Organic Compounds. McGraw-Hill Book Co., New York.

MORIGUCHI, I. 1975. Quantitative structure-activity studies: I. Parameters relating to hydrophobicity. Chem. and Pharm. Bull. 23(2): 247-257.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH). 1973. Criteria for a Recommended Standard -- Occupational Exposure to Toluene. Washington, D.C. DHEW Publication No. (NIOSH) HSM 73-11023.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH). 1983. Registry of Toxic Effects of Chemical Substances. Data Base. Washington, D.C. October 1983.

NATIONAL RESEARCH COUNCIL (NRC). 1980. The Alkyl Benzenes. National Academy Press, Washington, D.C.

OVERCASH, M.R., J.B. WEBER and M.L. MILES. 1982. Behavior of Organic Priority Pollutants in the Terrestrial System: Di-N-butyl phthalate ester, toluene and 2,4-dinitrotoluene. Publ. Report 171, Water Resources Research Institute, Univ. of North Caroline. NTIS PB82-224544.

PAVLOU, S.P. 1980. Thermodynamic Aspects of Equilibrium Sorption of Persistent Organic Molecules at the Sediment-Seawater Interface: A Framework For Predicting Distributions in the Aquatic Environment. IN: Contaminants and Sediments. Volume 2. Baker, R.A. (Editor). Science Publishers, Inc. Ann Arbor, MI.

SAX, N.I. 1975. Dangerous Properties of Industrial Materials. 4th ed. Van Nostrand Reinhold Co., New York. 1,258 pages.

TEWARI, Y.B., MILLER, M.M. WASIK, S.P. AND D.E. MARTIRE. 1982. Aqueous solubility and octanol/water partition coefficient of organic compounds at 25°C. J. Chem. Eng. Data. 27:451-454.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1979. Water-Related Environmental Fate of 129 Priority Pollutants. Washington, D.C. December 1079. EPA 440/4-79-029.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1980. Ambient Water Quality Criteria for Toluene. Office of Water Regulations and Standards, Criteria and Standards Division. Washington D.C. October 1980. EPA 440/5-80-075.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1984. Health Effects Assessment for Toluene. Final Draft. Environmental Criteria and Assessment Office, Cincinatti, Ohio. September 1984. ECAO-CIN-H033.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1985. Draft Superfund Public Health Evaluation Manual. Prepared by: ICF Incorporated, Washington D.C. USEPA Office of Solid Waste and Emergency Response, Washington D.C. EPA Contract No. 68-01-7090.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1986a. Quality Criteria for Water, 1986 ("The Gold Book"). Office of Water Regulations and Standards, Washington, DC. EPA 440/5-86-001.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1986b. Risk Reference Dose for Toluene. Integrated Risk Information System (IRIS). [Note: This is an EPA computerized data base.]

VALVANI, S.C., YALKOWSKY, S.H., and ROSEMAN, T.J. 1980. Solubility and partitioning. IV. Aqueous solubility and octanol-water partition coefficients of liquid nonelectrolytes. J. Pharm. Sci. 70 (5):502-202.

WEAST, R.E., ed. 1981. Handbook of Chemistry and Physics. 62nd ed. CRC Press, Cleveland, Ohio. 2332 pages.

WILSON, J.T., C.G. ENFIELD, W.J. DUNLAP, R.L. COLBY, D.A. FOSTER and L.B. BASKIN. 1981. Transport and Fate of Selected Organic Pollutants in a Sandy Soil. J. Environ. Qual. 10(4); 501-506.

1,1,1-TRICHLOROETHANE[1/]

Summary

Preliminary results suggest that 1,1,1-trichloroethane (1,1,1-TCA) induces liver tumors in female mice. It was shown to be mutagenic using the Ames assay (Salmonella), and in cultured rat embryo cells. Inhalation exposure to high concentrations of 1,1,1-TCA depresses the central nervous system, affects cardiovascular function, and damages the lungs, liver, and kidneys in animals and humans. Irritation of the skin and mucous membranes has also been associated with human exposures to 1,1,1-trichloroethane.

CAS Number: 71-55-6

Chemical Formula: CH_3CCl_3

IUPAC Name: 1,1,1-Trichloroethane

Important Synonyms and Trade Names: Methyl chloroform, chloro-1,1,1-TCA

Chemical and Physical Properties

Molecular Weight: 133.4

Boiling Point: 74.1°C

1/ Compiled From: U.S. Environmental Protection Agency, Office of Waste Program Enforcement. September 1985. Chemical, physical, and biological properties of compounds present at hazardous waste sites. A Final Report Prepared by Clement Associates, Inc., Arlington, Virginia.

Also: United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL). 1985. Physical, Chemical, and Toxicological Data Summaries of 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

Melting Point: --30.4°C

Specific Gravity: 1.34 at 20°C (liquid)

Solubility in Water: 4,400 mg/liter at 20°C (Verschueren 1977)

Solubility in Organics: Soluble in acetone, benzene, carbon tetrachloride, methanol, ether, alcohol, and chlorinated solvents

Log Octanol/Water Partition Coefficient (K_{ow}): 2.17
2.42 (Geyer et al. 1984)
2.47 (Davies and Dobbs, 1984)
2.49 (Hansch and Leo, 1979)
2.5 (Mabey et al. 1982)

Soil/Water Partition Coefficient (K_{oc}):

104	Chiou et al. (1979) Fig. 2 (experimental)
146 - 83	Lyman et al. (1982) Eqn 4-5 (S = 480 - 1,360)
1,000	Lyman et al. (1982) Eqn 4-8 (log K_{ow} = 3.0)
630	Lyman and Loreti (1986) Eqn I (log K_{ow} = 3.0)
630	Lyman and Loreti (1986) Eqn II (log K_{ow} = 3.0)
630	Lyman and Loreti (1986) Eqn III (log K_{ow} = 3.0)
897	Kadeg et al. (1986) (log K_{ow} = 3.0)

Bioconcentration Factor:

95	Davies and Dobbs (1984) Eqn B (log K_{ow} = 3.0
8	Davies and Dobbs Table 2 (experimental)
31.8	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 2.28)
32.4	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 2.29)
40.7	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 2.42)
190	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 3.3)
19-10.6	Davies and Dobbs (1984) Eqn A (S = 480-1,360)
23-82	Davies and Dobbs (1984) Eqn B (log K_{ow} = 2.3-3.3)
46	Davies and Dobbs (1984) Eqn B (log K_{ow} = 3.0)
110	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 3.0)

Vapor Pressure: 123 mm Hg at 20°C (USEPA 1985)
127 mm Hg at 25°C (TBD Peer Review Committee, 1984)

Vapor Density: 4.63

Henry's Law Constant: 0.044 atm-m^3/mole (calculated)
0.0144 atm-m^3/mole (USEPA 1985)

Transport and Fate

1,1,1-Trichloroethane (1,1,1-TCA) disperses from surface water primarily by volatilization. Following volatilization, photooxidation by reaction with hydroxyl radicals in the atmosphere is the principal fate process. Several studies have indicated that 1,1,1-trichloroethane may be adsorbed onto organic materials in the sediment. A range of experimental and estimated soil-water partition coefficients (K_{OC}) is reported above and indicates that some sorption of 1,1,1-trichloroethane to soils/sediments and dissolved organic material will occur. Pavlou (1980) estimates that sorption of volatiles organic compounds will range from low to moderate. The combined water solubility and organic partitioning data for 1,1,1-TCA suggest that this compound will exhibit some degree of environmental mobility.

A range of experimental and estimated bioconcentration factors (BCFs) for 1,1,1-trichloroethane is also reported above. ASTM (1985) indicates that chemicals with bioconcentration factors less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the concentration factors suggest that appreciable bioconcentration or biomagnification of 1,1,1-trichloroethane residues is not likely to occur.

Health Effects

1,1,1-trichloroethane has been retested for carcinogencity due to early lethality in a previous study by the National Cancer Institute (NCI, 1977). Preliminary results indicate that 1,1,1-trichloroethane increased the incidence of combined hepatocellular carcinomas and adenomas in female mice when administered by gavage (NTP 1984). There is evidence that 1,1,1-trichloroethane is mutagenic in Salmonella typhimurium and causes transformation in cultured rat embryo cells (USEPA 1980). These data suggest that the chemical may be carcinogenic.

Other toxic effects of 1,1,1-trichloroethane are seen only at concentrations well above that likely in an open environment. The most notable toxic effects of 1,1,1-trichloroethane in humans and animals are central nervous system depression, including anesthesia at very high concentrations and impairment of coordination, equilibrium, and judgment at lower concentrations (350 ppm and above); cardiovascular effects, including premature ventricular contractions, decreased blood pressure, and sensitization to epinephrine-induced arrhythmia and adverse effects on the lungs, liver, and kidneys. Irritation of the skin and mucous membranes resulting from exposure to 1,1,1-trichloroethane has also been reported. The oral LD_{50} value of 1,1,1-trichloroethane in rats is approximately 11,000 mg/kg.

Toxicity to Wildlife and Domestic Animals

The acute toxicity of 1,1,1-trichloroethane to aquatic species is rather low, with the LC_{50} concentration for the most sensitive species tested being 52.8 mg/l. No chronic toxicity studies have been conducted on 1,1,1-trichloroethane, but acute-chronic ratios for the other chlorinated ethanes ranged from 2.8 to 8.7.

The acute oral LD_{50} values for 1,1,1-trichloroethane in rabbits and dogs are 5,660 mg/kg and 750 mg/kg, respectively (Sax, 1979).

Regulations and Standards

Ambient Water Quality Criteria (USEPA 1986):

The available data are not adequate for establishing criteria. However, EPA does report the lowest values of the two trichloroethanes (1,1,1 and 1,1,2) known to be toxic in aquatic organisms.

Aquatic Life (Freshwater)

Acute toxicity: 18 mg/liter
Chronic toxicity: No available data

Aquatic Life (Saltwater)

Acute toxicity: 31.2 mg/liter
Chronic toxicity: No available data

Human Health

Criterion: 18.4 mg/liter

National Primary Drinking Water Standard (USEPA): 0.20 mg/liter (Proposed MCL; 50 Federal Register 46904, Wednesday November 13, 1985).

NIOSH Recommended Standard: Ceiling Level = 350 ppm (1,910 mg/m^3/15 min

OSHA Standard: TWA[1/] = 350 ppm (1,910 mg/m^3)

1/ Time Weighted Average.

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

For 1,1,1-trichloroethane (TCA) the D_T value is derived from the data used to establish an EPA-proposed Maximum Contaminant Level (MCL) (50 Federal Register 46904, Wednesday November 13, 1985; see also USEPA 1985). The proposed MCL is based on a subchronic inhalation study utilizing mice, rats, dogs, and monkeys exposed continuously for up to 14 weeks (McNutt et al. 1975). Cytoplasmic alterations in centrilobular hepatocytes occurred in mice of the high dose group (5,400 mg/m^3); mild to minimal cytoplasmic alterations were seen in the liver cells of mice in the low dose group (1,350 mg/m^3 or 35 mg/kg/day). No effects were seen in exposed rats, dogs, or monkeys. The identified Lowest-Observed-Adverse-Effect-Level (LOAEL) from this study utilizing the mouse as the sensitive species is therefore 35 mg/kg/day. An Uncertainty Factor (UF) of 1,000 is employed to address the extrapolation of results to humans (10), use of a LOAEL rather than a NOEL) (10) and to account for the use of a subchronic rather than a chronic experimental exposure period (10). Derivation of the D_T value for 1,1,1-trichloroethane is as follows:

$$D_T = \frac{\text{LOAEL (mg/kg/day)}}{\text{UF}}$$

$$= \frac{35}{1{,}000}$$

$$= 0.035 \text{ mg/kg/day}$$

REFERENCES

ASTM. 1985. Standard Practice for conducting bioconcentration tests with fishes and saltwater bivalve mollusca. Designation E 1022-84, pages 590-62. In: 1985 Annual Book of ASTM Standards Volume 11.04. American Society for Testing and Materials, Philadelphia, Pennsylvania.

CHIOU, C.T., PETERS, L.J., and FREED, V.H. 1979. A physical concept of soil-water equilibria for nonionic organic compounds. Science. 206:831-832.

DAVIES, R.P. and DOBBS, A.J. 1984. The prediction of bioconcentration in fish. Water Res. 18(10): 1253-1262.

GEYER, H., G. POLITZKI and D. FREITAG. 1984. Prediction of ecotoxicological behavior of chemicals: relationship between n-octanol/water partition coefficient and bioaccumulation of organic chemicals by Alga Chlorella. Chemosphere, 13(2):269-284.

HANSCH, C, and LEO, A.J. 1979. Substituent constants for correlation analysis in chemistry and biology. John Wiley and Sons, New York, NY.

INTERNATIONAL AGENCY FOR RESEARCH ON CANCER (IARC). 1979. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. Vol. 20: Some Halogenated Hydrocarbons. World Health Organization, Lyon, France. Pp. 515-531.

KADEG, R.D., PAVLOU, S.P. and DUXBURY, A.S. 1986. Elaboration of Sediment Normalization Theory for Non Polar Hydrophobic Organic Chemicals. U.S. Environmental Protection Agency, Criteria and Standards Division, Washington D.C.

LYMAN, W.J., W.F. REEHL and D.H. ROSENBLATT. 1982. Handbook of Chemical Property Estimation Methods: Environmental Behavior of Organic Compounds. McGraw-Hill Book, Co., New York, NY.

LYMAN, W.J. and LORETI, C.P. 1986. Prediction of Soil and Sediment Sorption for Organic Compounds (Comment Final Draft). U.S. Environmental Protection Agency, Monitoring and Data Support Division, Office of Water Regulations and Standards. Washington D.C.

MCNUTT, N.S., AMSTER, R.L., MCCONNELL, E.E., AND MORRIS, F. 1975. Hepatic lesions in mice after continuous inhalation exposure to 1,1,1-trichlorethane. Lab. Invest. 32:642-654.

NATIONAL CANCER INSTITUTE (NCI). 1977. Bioassay of 1,1,1-Trichloroethane for Possible Carcinogenicity. CAS No. 71-55-6. NCI Carcinogenesis Technical Report Series No. 3. Washington, D.C. DHEW Publication No. (NIH) 77-803.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH). 1976. Criteria for a Recommended Standard--Occupational Exposure to 1,1,1-Trichloroethane (Methyl Chloroform). Washington, D.C. DHEW Publication NO. (NIOSH) 76-184.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH). 1983. Registry of Toxic Effects of Chemical Substances. Data Base. Washington, D.C. October 1983.

NATIONAL TOXICOLOGY PROGRAM (NTP). 1984. Annual Plan for Fiscal Year 1984. Research Triangle Park, N.C. DHHS Public Health Service. NTP-84-023.

PAVLOU, S.P. 1980. Thermodynamic Aspects of Equilibrium Sorption of Persistent Organic Molecules at the Sediment-Seawater Interface: A Framework For Predicting Distributions in the Aquatic Environment. IN: Contaminants and Sediments. Volume 2. Baker, R.A. (Editor). Science Publishers, Inc. Ann Arbor, MI.

SAX, I.N. 1979. Dangerous Properties of Industrial Materials. Fifth Edition. Van Nostrand Reinhold Company, New York. 1118 pages.

TDB PEER REVIEW COMMITTEE. 1984. Toxicology Data Bank, National library of Medicine and National Institute of Health, Department of Health and Human Services, Washington, D.C. (Computerized Data Base).

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1979. Water-Related Environmental Fate of 129 Priority Pollutants. Washington D.C. December 1979. EPA 440/4-79-029.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1980. Ambient Water Quality Criteria for Chlorinated Ethanes. Office of Water Regulations and Standards, Criteria and Standards Division. Washington, D.C. October 1980. EPA 440/5-80-029.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1984. Health Effects Assessment for 1,1,1-Trichloroethane. Environmental Criteria and Assessment Office, Cincinnati, Ohio. September 1984. ECAO-CIN-H005 (Final Draft).

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1984. Health Assessment Document for 1,1,1-Trichloroethane (Methyl Chloroform). Final Report. Office of Health and Environmental Assessment. Washington, D.C. EPA No. EPA-600/8-82-003F.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1985. Draft Health Advisory for 1,1,1-Trichloroethane. Office of Drinking Water. USEPA, Washington, D.C. September 30, 1985.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1986. Quality Criteria for Water, 1986 ("The Gold Book"). Office of Water Regulations and Standards, Washington, DC. EPA 440/5-86-001.

VEITH, G.D., D.J. CALL and L.T. BROOKE. 1983. Structure-toxicity relationships for the fathead minnow, Pimephales promelas: narcotic industrial chemicals. Can J. Fish Aquat. Sci., 40:743-748.

VERSCHUEREN, K. 1977. Handbook of Environmental Data on Organic Chemicals. Van Nostrand Reinhold Co., New York. 659 pages.

WEAST, R.E., ed. 1981. Handbook of Chemistry and Physics. 62nd ed. CRC Press, Cleveland, Ohio. 2,332 pages.

1,1,2-TRICHLOROETHANE[1/]

Summary

1,1,2-Trichloroethane (1,1,2-TCA) induced liver tumors and pheochromocytomas of the adrenal gland in mice. Liver and kidney damage occurred in dogs subacutely exposed (i.p.) to 1,1,2-TCA. It was not mutagenic when tested with the Ames (Salmonella) assay.

CAS Number: 79-00-5

Chemical Formula: $CH_2ClCHCl_2$

IUPAC Name: 1,1,2-Trichloroethane

Important Synonyms and Trade Names: Vinyl trichloride, ethane trichloride

Chemical and Physical Properties

Molecular Weight: 133.41

Boiling Point: 133.8°C
114°C (TBD Peer Review Committee, 1984)

Melting Point: -36.5°C

1/ Compiled From: U.S. Environmental Protection Agency, Office of Waste Program Enforcement. September 1985. Chemical, physical, and biological properties of compounds present at hazardous waste sites. A Final Report Prepared by Clement Associates, Inc., Arlington, Virginia.

Also: United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL). 1985. Physical, Chemical, and Toxicological Data Summaries of 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

Specific Gravity: 1.4397 at 20°C

Solubility in Water: 4,500 mg/liter at 20°C

Solubility in Organics: Soluble in alcohol, ether, and chloroform

Log Octanol/Water Partition Coefficient (K_{ow}): 2.17
2.07 (Lyman et al., 1982) Fragment Method.

Soil/Water Partition Coefficient (K_{oc}):

43	Lyman et al. (1982) Eqn 4-5 (S = 4,400)
318	Lyman et al. (1982) Eqn 4-8 (log K_{ow} = 2.07)
118	Lyman and Loreti (1986) Eqn I (log K_{ow} = 2.07)
106	Lyman and Loreti (1986) Eqn II (log K_{ow} = 2.07)
108	Lyman and Loreti (1986) Eqn III (log K_{ow} = 2.07)
193	Kadeg et al. (1986) (log K_{ow} = 2.07)

Bioconcentration Factor:

22.0	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 2.07)
5.4	Davies and Dobbs (1984) Eqn A (S = 4,400)
16	Davies and Dobbs (1984) Eqn C (log K_{ow} = 2)
24	Davies and Dobbs (1984) Eqn B (log K_{ow} = 2)
15.3	Davies and Dobbs (1984) Eqn C (log K_{ow} = 2.07)
26.5	Davies and Dobbs (1984) Eqn B (log K_{ow} = 2.07)

Vapor Pressure: 19 mm Hg at 20°C
20 mm Hg at 21.6°C (Perry and Chilton, 1973)
23.5 mm Hg at 25°C (Estimated; Lyman et al., 1982)

Vapor Density: 4.63

Henry's Law Constant: 9×10^{-4} atm-m^3/mole (calculated)
1.17×10^{-3} atm-m^3/mole (USEPA 1985)

Transport and Fate

Volatilization and subsequent photooxidation in the troposphere are probably the primary transport and fate processes for 1,1,2-trichloroethane in aqueous media. A range of estimated

soil-water partition coefficients (K_{OC}) is reported above and indicates that some sorption of 1,1,2-trichloroethane to soils/sediments and dissolved organic material will occur. Pavlou (1980) estimates that sorption of volatile organic compounds will range from low to moderate. The combined high water solubility and low organic partitioning suggests that 1,1,2-trichloroethane will exhibit a high degree of environmental mobility.

A range of estimated bioconcentration factors (BCFs) for 1,1,2-trichloroethane is also reported above. ASTM (1985) indicates that chemicals with bioconcentration factors less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the concentration factors suggest that appreciable bioconcentration or biomagnification of 1,1,2-trichloroethane residues is not likely to occur.

Health Effects

1,1,2-Trichloroethane was not mutagenic when tested in Salmonella (NTP 1985). It induced heptacellular carcinomas and pheochromocytoma of the adrenal gland following oral exposure (78 weeks) in male and female mice but did not produce a significant increase in tumor incidence in male or female rats (NCI 1977). EPA has classified 1,1,2-trichloroethane according to EPA's Guidelines for Carcinogenic Risk Assessment in EPA's Group C (possible human carcinogen) based on positive evidence in mice and an absence of data on humans.

No information was found concerning the reproductive toxicity or teratogenicity of 1,1,2-trichloroethane. No chronic studies were found other than the carcinogensis bioassay identified above which addressed the toxicity of 1,1,2-trichloroethane; however, single doses as low as 400 mg/kg caused liver and kidney damage in dogs. The oral LD_{50} value for 1,1,2-trichloroethane in rats is 835 mg/kg.

Toxicity to Wildlife and Domestic Animals

The acute LC_{50} values for 1,1,2-trichloroethane for freshwater aquatic organisms ranged from 18,000 to 81,700 µg/liter. One chronic test indicated that the acute-chronic ratio for 1,1,2-trichloroethane was approximately 8.7. No information on the toxicity of 1,1,2-trichloroethane to saltwater species, terrestrial wildlife, or domestic animals was available in the literature reviewed.

Regulations and Standards

Ambient Water Quality Criteria (USEPA 1986):

The available data are not sufficient for establishing criteria. However, EPA does report the lowest values known to be toxic in aquatic organisms.

Aquatic Life (Freshwater)

Acute toxicity: 18,000 µg/liter (1,1,1 and 1,1,2 - TCA)
Chronic toxicity: 9,400 µg/liter

Aquatic Life (Saltwater)

Acute toxicity: No available data
Chronic toxicity: No available data

Human Health

Due to the carcinogenicity of 1,1,2-trichloroethane the ambient water criterion is set at zero. However, estimates of the carcinogenic risks associated with lifetime exposure from ingestion of contaminated water and aquatic organisms are:

Risk	Concentration
10^{-5}	6.0 µg/liter
10^{-6}	0.6 µg/liter
10^{-7}	0.06 µg/liter

CAG Potency Slope for oral exposure (USEPA 1985): 5.73×10^{-2} $(mg/kg/day)^{-1}$

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

For carcinogens such as 1,1,2-trichloroethane, the D_T value is based on the USEPA Cancer Assessment Group's cancer potency slope. The cancer potency slopes have been estimated for oral exposure routes and for inhalation exposure for some chemicals. The slopes are intended to be a plausible upper bound of the potency of a carcinogen in inducing cancer at low doses. Calculation of a D_T using a cancer potency slope requires selection of an acceptable cancer risk level. A range of risk levels from 10^{-4} to 10^{-7} is considered for all carcinogens, therefore a range of D_T values is presented. Derivation of the D_T values for 1,1,2-trichloroethane is as follows:

$$D_T = \frac{\text{Risk Level}}{\text{Potency Slope}} \ (mg/kg/day)^{-1}$$

$$= \frac{1 \times 10^{-4}}{5.73 \times 10^{-2}} \ (mg/kg/day)^{-1}$$

$$= 1.7 \times 10^{-3} \text{ mg/kg/day}$$

The range of D_T values for 1,1,2-trichloroethane is presented below:

Risk Level	D_T (mg/kg/day)
10^{-4}	1.7×10^{-3}
10^{-5}	1.7×10^{-4}
10^{-6}	1.7×10^{-5}
10^{-7}	1.7×10^{-6}

REFERENCES

ASTM. 1985. Standard Practice for conducting bioconcentration tests with fishes and saltwater bivalve mollusca. Designation E 1022-84, pages 590-62. In: 1985 Annual Book of ASTM Standards Volume 11.04. American Society for Testing and Materials, Philadelphia, Pennsylvania.

CHIOU, C.T., PETERS, L.J., and FREED, V.H. 1979. A physical concept of soil-water equilibria for nonionic organic compounds. Science. 206:831-832.

DAVIES, R.P. and A.J. DOBBS. 1984. The prediction of bioconcentration in fish. Water Res. 18(10):1253-1262.

INTERNATIONAL AGENCY FOR RESEARCH ON CANCER (IARC). 1979. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. Vol. 20: Some Halogenated Hydrocarbons. World Health Organization, Lyon, France. Pp. 533-543.

KADEG, R.D., PAVLOU, S.P., DUXBURY, A.S. 1986. Elaboration of Sediment Normalization Theory for Non Polar Hydrophobic Organic Chemicals. U.S. Environmental Protection Agency, Criteria and Standards Division, Washington D.C.

LYMAN, W.J., LQRETI, C.P. 1986. Prediction of Soil and Sediment Sorption for Organic Compounds (Comment Final Draft). U.S. Environmental Protection Agency, Monitoring and Data Support Division, Office of Water Regulations and Standards. Washington D.C.

LYMAN, W.J., REEHL, W.F., and ROSENBLATT, D.H. 1982. Handbook of Chemical Property Estimation Methods: Environmental Behavior of Organic Compounds. McGraw-Hill Book Co., New York.

NATIONAL CANCER INSTITUTE (NCI). 1977. Bioassay of 1,1,2-Trichloroethane for Possible Carcinogenicity. CAS No. 79-00-5. NCI Carcinogenesis Technical Report Series No. 74. Washington, D.C. DHEW Publication No. (NIH) 78-1324.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH). 1983. Registry of Toxic Effects of Chemical Substances. Data Base. Washington, D.C. October 1983.

NATIONAL TOXICOLOGY PROGRAM (NTP). 1985. Fiscal Year 1985 Annual Plan. U.S. Public Health Service, Department of Health and Human Services. Washington, D.C. NTP-85-055. March 1985.

PAVLOU, S.P. 1980. Thermodynamic Aspects of Equilibrium Sorption of Persistent Organic Molecules at the Sediment-Seawater Interface: A Framework For Predicting Distributions in the Aquatic Environment. IN: Contaminants and Sediments. Volume 2. Baker, R.A. (Editor). Science Publishers, Inc. Ann Arbor, MI.

PERRY, R.H. and CHILTON, C.H. 1973. Chemical Engineer's Handbook, 5th Edition. McGraw-Hill Book Co., New York, NY.

TDB PEER REVIEW COMMITTEE. 1984. Toxicology Data Bank, National library of Medicine and National Institutes of Health, Department of Health and Human Services, Washington, D.C. (Computerized Data Base).

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1979. Water-Related Environmental Fate of 129 Priority Pollutants. Washington D.C. December 1979. EPA 440/4-79-029.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1980. Ambient Water Quality Criteria for Chlorinated Ethanes. Office of Water Regulations and Standards, Criteria and Standards Division, Washington, D.C. October 1980. EPA 440/5-80-029.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1984. Health Effects Assessment for 1,1,2-Trichloroethane. Environmental Criteria and Assessment Office, Cincinnati, Ohio. September 1984. ECAO-CIN-H045 (Final Draft).

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1985. Draft Superfund Public Health Evaluation Manual. Prepared by: ICF Incorporated, Washington D.C. USEPA Office of Solid Waste and Emergency Response, Washington D.C. EPA Contract No. 68-01-7090.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1986. Quality Criteria for Water, 1986 ("The Gold Book"). Office of Water Regulations and Standards, Washington, DC. EPA 440/5-86-001.

VERSCHUEREN, K. 1977. Handbook of Environmental Data on Organic Chemicals. Van Nostrand Reinhold Co., New York. 659 pages.

WEAST, R.E., ed. 1981. Handbook of Chemistry and Physics. 62nd ed. CRC Press, Cleveland, Ohio. 2,332 pages.

TRICHLOROETHYLENE[1/]

Summary

Trichloroethylene (TCE) induced hepatocellular carcinomas in mice following oral administration and was mutagenic when tested using several microbial assay systems. Chronic inhalation exposure to high concentrations caused liver, kidney, and neurological damage and dermatological irritation in animals.

CAS Number: 79-01-6

Chemical Formula: C_2HCl_3

IUPAC Name: Trichloroethylene

Important Synonyms and Trade Names: Trichloroethylene, TCE, and ethylene trichloride

Chemical and Physical Properties

Molecular Weight: 131.5

Boiling Point: 87°C

Melting Point: -73°C

Specific Gravity: 1.4642 at 20°C

1/ Compiled From: U.S. Environmental Protection Agency, Office of Waste Program Enforcement. September 1985. Chemical, physical, and biological properties of compounds present at hazardous waste sites. A Final Report Prepared by Clement Associates, Inc., Arlington, Virginia.

Also: United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL). 1985. Physical, Chemical, and Toxicological Data Summaries of 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

Solubility in Water: 1,100 mg/liter (USEPA 1985a)
825 mg/liter (Valvani et al., 1980)

Solubility in Organics: Soluble in alcohol, ether, acetone, and chloroform

Log Octanol/Water Partition Coefficient (K_{ow}): 2.29 (Hansch and Leo 1979)
2.29 (Rogers et al., 1980)
2.42 (Veith et al., 1983)
2.53 (Tewari et al., 1982)
3.24 (Geyer et al., 1984)
3.3 (Valvani et al., 1980)

Soil/Water Partition Coefficient (K_{oc}):

109; 93	Lyman et al. (1982) Eqn 4-5 (S = 825; 1,100)
188	Rogers et al. (1980) Table V (experimental)
420; 494	Lyman et al. (1982) Eqn 4-8 (log K_{ow} = 2.29 - 2.42)
1,490; 414	Lyman et al. (1982) Eqn 4-8 (log K_{ow} = 3.3; 2.28)
290	Lyman and Loreti (1986) Eqn I (log K_{ow} = 2.57)
276	Lyman and Loreti (1986) Eqn II (log K_{ow} = 2.57)
279	Lyman and Loreti (1986) Eqn III (log K_{ow} = 2.57)
441	Kadeg et al. (1986) (log K_{ow} = 2.57)

Bioconcentration Factor:

95	Davies and Dobbs (1984) Eqn B (log K_{ow} = 3)
17	Kenaga (1980) Table 3 (experimental)
17	Davies and Dobbs Table 2 (experimental)
31.8	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 2.28)
32.4	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 2.29)
40.7	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 2.42)
189.7	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 3.3)
14	Davies and Dobbs (1984) Eqn A (S = 825)
27.5	Davies and Dobbs (1984) Eqn C (log K_{ow} = 2.57)
52.8	Davies and Dobbs (1984) Eqn B (log K_{ow} = 2.57)
52.9	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 2.57)

Vapor Pressure: 60 mm Hg at 20°C
57.9 mm Hg at 25°C (USEPA 1985a)

Vapor Density: 4.53

Henry's Law Constant: 1.3×10^{-2} atm-m^3/mole (calculated)
9.1×10^{-3} atm-m^3/mole (USEPA 1985a)

Transport and Fate

Trichloroethylene (TCE) rapidly volatilizes into the atmosphere from surface waters and soil surfaces where it reacts with hydroxyl radicals to produce hydrochloric acid, carbon monoxide, carbon dioxide, and carboxylic acid. The atmospheric lifetime of TCE estimated on the basis of reactions with hydroxyl radicals is 54 hours (USEPA 1985b).

A range of experimental and estimated soil-water partition coefficients (K_{oc}) is reported above and indicates that some sorption of trichloroethylene to soils/sediments and dissolved organic material will occur. Pavlou (1980) estimates that sorption of volatile organic compounds will range from low to moderate. The combined water solubility and organic partitioning of trichlorethylene suggests that this compound will exhibit some degree of environmental mobility. There is evidence that microorganisms can metabolize TCE; however, it is unclear whether trichloroethylene bound to organic materials can be transformed directly or whether it must be desorbed in order to be degraded.

A range of experimental and estimated bioconcentration factors (BCFs) for trichloroethylene is also reported above. ASTM (1985) indicates that chemicals with bioconcentration factors less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the concentration factors suggests that appreciable bioconcentration or biomagnification of trichloroethylene residues is not likely to occur.

Health Effects

Trichloroethylene was mutagenic in tests using several microbial assay systems. It was carcinogenic in mice producing hepatocellular carcinomas following oral administration (NCI 1976, NTP 1982).

Trichloroethylene has been classified according to EPA's Guidelines for Carcinogenic Risk Assessment in EPA's Group B2 (probable human carcinogen), based on the finding of liver tumors in orally exposed mice and inadequate evidence in humans (USEPA 1985b).

Embryo toxicity occurred in rats exposed via inhalation to TCE at 1,800 ppm for 2 weeks prior to mating and during days 1-20 of gestation (USEPA 1985b). Inhalation for 3 weeks prior to mating and during gestation days 1-18 (rat) and during gestation days 1-21 (rabbit) also resulted in embryo toxicity. TCE has been shown to cause renal toxicity, hepatotoxicity, neurotoxicity, and dermatological reactions in animals following chronic exposure to levels greater than 2,000 mg/m^3 for 6 months (USEPA 1985b). The acute oral LD_{50} value of trichloroethylene in the rat is 4,920 mg/kg and 2,402 mg/kg in the mouse.

In humans, chronic exposure is characterized by dizziness, nausea, headache, ataxia, decreased appetite and sleep disturbances (USEPA 1985b). Effects of short-term exposure include mild eye irritation, nausea, vertigo, headache and confusion. Unconsciousness and death may occur following exposure to excessive concentrations (USEPA 1985b).

Toxicity to Wildlife and Domestic Animals

Only limited data was available on the toxicity of trichloroethylene to aquatic organisms. The acute toxicity to freshwater species was similar in the three species tested, with LC_{50} values of about 50 mg/liter (USEPA 1980). No LC_{50} values were available for saltwater species (USEPA 1980). However, 2 mg/liter caused erratic swimming and loss of equilibrium in the grass shrimp. No chronic toxicity tests were reported.

No information on the toxicity of trichloroethylene to domestic animals or terrestrial wildlife was available in the literature reviewed.

Regulations and Standards

Ambient Water Quality Criteria (USEPA 1986):

The available data are not adequate for establishing criteria. However, EPA does report the lowest values known to be toxic in aquatic organisms.

Aquatic Life (Freshwater)

Acute toxicity: 45 mg/liter
Chronic toxicity: 21.9 mg/liter

Aquatic Life (Saltwater)

Acute toxicity: 2 mg/liter
Chronic toxicity: No available data

Human Health

Due to the carcinogenicity of trichloroethylene the ambient water criterion is set at zero. Estimates of the carcinogenic risks associated with lifetime exposure from ingestion of contaminated water and contaminated aquatic organisms are:

Risk	Concentration
10^{-5}	27 mg/liter
10^{-6}	2.7 mg/liter
10^{-7}	0.27 mg/liter

National Primary Drinking Water Standard (USEPA): 0.005 mg/liter (Proposed MCL; 50 Federal Register 46904 Wednesday November 13, 1985).

CAG Potency Slope for Oral Exposure (USEPA 1985b): 1.1×10^{-2} $(mg/kg/day)^{-1}$

CAG Potency Slope for Inhalation Exposure (USEPA 1985b): 4.6×10^{-3} $(mg/kg/day)^{-1}$

NIOSH Recommended Standards (air): TWA[1/] = 540 mg/m^3
Ceiling Level = 760 mg/m^3 10-min

OSHA Standards (air): TWA = 540 mg/m^3
Ceiling Level = 1,075 mg/m^3/15-min
Peak Concentration = 1,620 mg/m^3 for 5 min every 3 hr,

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

For carcinogens such as trichloroethylene, the D_T value is based on the USEPA Cancer Assessment Group's cancer potency slopes. The cancer potency slopes have been estimated for oral exposure routes and for inhalation exposure for trichloroethylene. The slopes are intended to be a plausible upper bound of the potency of a carcinogen in inducing cancer at low doses. Calculation of a D_T using a cancer potency slope requires selection of an acceptable cancer risk level. A range of risk levels from 10^{-4} to 10^{-7} will be considered for all carcinogens, therefore a range of D_T values is presented. Derivation of the D_T values for trichloroethylene is as follows:

$$D_T = \frac{\text{Risk Level}}{\text{Potency Slope } (mg/kg/day)^{-1}}$$

$$= \frac{1 \times 10^{-4}}{1.1 \times 10^{-2} (mg/kg/day)^{-1}}$$

$$= 9.1 \times 10^{-3} \text{ mg/kg/day}$$

1/ Time Weighted Average.

The range of D_T-values for trichloroethylene is presented below.

Risk Level	Oral D_T (mg/kg/day)	Inhalation D_T (mg/kg/day)
10^{-4}	9.1×10^{-3}	2.2×10^{-2}
10^{-5}	9.1×10^{-4}	2.2×10^{-3}
10^{-6}	9.1×10^{-5}	2.2×10^{-4}
10^{-7}	9.1×10^{-6}	2.2×10^{-5}

REFERENCES

ASTM. 1985. Standard Practice for conducting bioconcentration tests with fishes and saltwater bivalve mollusca. Designation E 1022-84, pages 590-62. In: 1985 Annual Book of ASTM Standards Volume 11.04. American Society for Testing and Materials, Philadelphia, Pennsylvania.

DAVIES, R.P. and A.J. DOBBS. 1984. The prediction of bioconcentration in fish. Water Res. 18(10):1253-1262.

GEYER, H., G. POLITZKI and D. FREITAG. 1984. Prediction of ecotoxicological behavior of chemicals: relationship between n-octanol/water partition coefficient and bioaccumulation of organic chemicals by Alga Chlorella. Chemosphere, 13(2):269-284.

HANSCH, C, and LEO, A.J. 1979. Substituent constants for correlation analysis in chemistry and biology. John Wiley and Sons, New York, NY.

INTERNATIONAL AGENCY FOR RESEARCH ON CANCER (IARC). 1979. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. Vol. 20: Some Halogenated Hydrocarbons. World Health Organization, Lyon, France. Pp. 545-572.

LYMAN, W.J., LORETI, C.P. 1986. Prediction of Soil and Sediment Sorption for Organic Compounds (Comment Final Draft). U.S. Environmental Protection Agency, Monitoring and Data Support Division, Office of Water Regulations and Standards. Washington D.C.

LYMAN, W.J., REEHL, W.F., and ROSENBLATT, D.H. 1982. Handbook of Chemical Property Estimation Methods: Environmental Behavior of Organic Compounds. McGraw-Hill Book Co., New York.

NATIONAL CANCER INSTITUTE (NCI). 1976. Bioassay of Trichloroethylene for Possible Carcinogenicity. CAS NO. 79-01-6. NCI Carcinogenesis Technical Report Series No. 2, Washington, D.C.. DHEW Publication NO. (NIH) 76-802.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH). 1983. Registry of Toxic Effects of Chemical Substances. Data Base. Washington, D.C. October 1983.

NATIONAL TOXICOLOGY PROGRAM (NTP). 1982. Carcinogenesis Bioassay of Trichloroethylene. CAS NO. 79-01-6. NTP 81-84, NIH Publication No. 82-1799.

PAVLOU, S.P. 1980. Thermodynamic Aspects of Equilibrium Sorption of Persistent Organic Molecules at the Sediment-Seawater Interface: A Framework For Predicting Distributions in the Aquatic Environment. IN: Contaminants and Sediments. Volume 2. Baker, R.A. (Editor). Science Publishers, Inc. Ann Arbor, MI.

ROGERS, R.D., J.C. McFARLANE, and A.J. CROSS. 1980. Adsorption and desorption of benzene in two soils and montmorillonite clay. Environ. Sci. Technol. 14(4):457-460.

TEWARI, Y.B., M.M. MILLER, S.P. WASIK and D.E. MARTIRE. 1982. Aqueous solubility and octanol/water partition coefficient of organic compounds at 25°C. J. Chem. Eng. Data, 27:451-454.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1979. Water-Related Environmental Fate of 129 Priority Pollutants. Washington D.C. December 1979. EPA 440/4-79-029.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1980. Ambient Water Quality Criteria for Trichloroethylene. Office of Water Regulations and Standards, Criteria and Standards Division, Washington, D.C. October 1980. EPA 440/5-80-077.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1984. Health Effects Assessment for Trichloroethylene. Final Draft. Environmental Criteria and Assessment Office, Cincinnati, Ohio. September 1984. ECAO-CIN-H009.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1985a. Draft Superfund Public Health Evaluation Manual. Prepared by ICF Incorporated, Washington, D.C. USEPA Office of Solid Waste and Emergency Response, Washington, D.C. EPA Contract No. 68-01-7090.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1985b. Health Assessment Document for Trichloroethylene. Final Report. Office of Health and Environmental Assessment. Washington, D.C. EPA 600/8-82-006F.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1986. Quality Criteria for Water, 1986 ("The Gold Book"). Office of Water Regulations and Standards, Washington, DC. EPA 440/5-86-001.

VERSCHUEREN, K. 1977. Handbook of Environmental Data on Organic Chemicals. Van Nostrand Reinhold Co., New York. 659 pages.

VALVANI, S.C., YALKOWSKY, S.H., and ROSEMAN, T.J. 1980. Solubility and partitioning. IV. Aqueous solubility and octanol-water partition coefficients of liquid nonelectrolytes. J. Pharm. Sci. 70 (5):502-202.

VEITH, G.D., D.J. CALL and T.L. BROOKE. 1983. Structure-toxicity relationships for the fathead minnow, Pimephales promelos: Narcotic Industrial Chemicals. Can. J. Fish Aquat. Sci., 40:743-748.

WATERS, R.E., ed. 1981. Handbook of Chemistry and Physics. 62nd ed. CRC Press, Cleveland, Ohio. 2,332 pages.

WEAST, R.E., ed. 1981. Handbook of Chemistry and Physics. 62nd ed. CRC Press, Cleveland, Ohio. 2,332 pages.

TRIMETHYLPHOSPHATE[1/]

Summary

Trimethylphosphate (TMP) is an alkylating agent used as an additive in gasoline and an intermediate in the production of organophosphate compounds. It has been shown to cause sterility in a number of laboratory rodents. In subchronic and chronic (carcinogenicity) tests, body weight gain was significantly reduced in exposed animals. TMP is a known mutagen in bacterial systems and mammalian cell cultures. A National Cancer Institute bioassay (1978) revealed a significantly increased incidence of endometrial adenocarcinomas in exposed female mice. Results in rats were considered equivocal.

CAS Number: 512-56-1

Chemical Formula: $C_3H_9O_4P$

IUPAC Name: Trimethyl Phosphate

Important Synonyms and Trade Names: Methyl phosphate; TMP; Phosphoric acid, trimethyl ester

Chemical and Physical Properties

Molecular Weight: 140

Boiling Point: 197.2°C (Weast 1977)

Melting Point: -46°C (Weast 1977)

1/ Primary Source: Berkowitz, J.G., Goyer, M.M., Harris, J.C., Lyman, W.J., Horne, R.A.,Nelten, L.J. Harrison, J.E., and Rosenblatt, D.H. 1978. Literature Review--Problem definition studies on selected chemicals. Final Report. Vol. II. Chemistry, toxicology, and potential environmental effects on selected organic pollutants. Contract No. DAMD 17-77-C-7037, Arthur D. Little, Inc. Cambridge, MA (AD B052946L).

Solubility in Water: 1,000 g/liter (Cogley and Foy 1978)

Solubility in Organics: Soluble in ether. Slightly soluble in alcohol.

Log Octanol/Water Partition Coefficient (K_{ow}): 0.30 (Leo et al. 1971)

Soil Water Partition Coefficient (K_{oc}): Not Applicable

Bioconcentration Factor: Not Applicable

Vapor Pressure: 3.8 mm Hg at 25°C (Berkowitz et al. 1978)

Henry's Law Constant: Not Applicable

Transport and Fate

Little data is available on the transport or fate of TMP in environmental media. Hydrolysis does occur and varying half-life estimates for TMP in neutral water at 15°C have been extrapolated by Berkowitz et al. (1978) from original data by use of either Arrhenius parameters or linear regression. These estimated values were, respectively, <1 week 1/, <6 weeks 2/, ≅ 21 weeks 3/, 19 years 4/ and 25 years 4/ (Berkowitz et al. 1978). The ultimate hydrolysis product of TMP is inorganic phosphate (Berkowitz et al. 1978).

TMP is a relatively volatile impurity in a number of organophosphate pesticide formulations. Tuazon et al. (1986) indicate that reactions of TMP with OH radicals in the troposphere are significant, resulting in a calculated tropospheric residence time of approximately three days. Reaction of TMP with ozone is not thought to constitute an important atmospheric loss process (Tuazon et al. 1986).

1/ Original data from Hudson and Harper (1958).
2/ Original data from Domage and Masse (1959).
3/ Original data from McTigue and Renowden (1970).
4/ Original data from Barnard et al. (1961).

aquatic organisms. However, the high aqueous solubility (i.e., polar nature) of TMP would likely preclude appreciable bioconcentration and biomagnification.

Health Effects

In a subchronic range-finding study, male and female rats were orally administered TMP three times per week for a period of seven weeks at doses of 100, 147, 215, 316, 464, 681, 1,000 or 1,470 mg/kg/day. Mice were given doses of 147, 215, 316, 464, 681, 1,000, 1,470, or 2,150 mg/kg/day (National Cancer Institute 1978) . All rats of both sexes died at doses of 681 mg/kg/day and greater. At 464 mg/kg/day, mean body weight gain was reduced to 56-68 percent of controls. In mice, one female and five males died at the highest dose and two females died at 1,470 mg/kg/day. Body weight gain was slightly depressed in males at 681 mg/kg/day and greater. Male rats receiving pellet diets containing 0.5 percent TMP for nine weeks exhibited significantly lowered body weights, increased kidney weights and reduced absolute testes weights (Oishi et al. 1982). Erythrocyte counts and hemoglobin concentrations of these rats were also significantly reduced as were serum levels of the enzymes glutamate oxalate transaminase and glutamate pyruvate transaminase compared with controls.

TMP has caused functional sterility in exposed mice, rats and rabbits (Harbison et al. 1976; Jackson and Jones 1968; Jones and Jackson 1969). TMP administered by gavage to male rats for a period of five days resulted in a form of functional sterility involving spematids and spermatazoa. Motile sperm were rendered incompetent (Berkowitz et al. 1978 cite Harbison et al. 1976). Harbison proposes that TMP induces sterility through inhibition of the spermatozoan enzyme choline acetyl transferase, which subsequently affects spermatozoan motility and therefore their ability to fertilize (Berkowitz et al. 1978 cite Harbison et al. 1976). In a more recent study, rats were given 250 mg/kg TMP orally 5 days per week for 30 days or 6 days per week for 60 days (Hanna and Kerr 1981). Spermatozoa obtained from the epididymis of dosed rats (5 days/week) were

abnormal. These sperm exhibited detached heads, abnormal heads, and abnormal middle and principal "pieces." Testes of these rats exhibited impaired spermatogenesis. Rats treated for 6 days per week had no cells in the seminiferous tubules which lead to collapse and shrinkage.

TMP is mutagenic in a number of test systems. It has produced chromosomal aberrations in cultured human lymphocytes (Soderman 1972) rat bone marrow cultures (Adler et al. 1971) and dominant lethal effects in mice (Epstein et al. 1970). Positive results (heritable genetic alterations) have also been obtained in bacterial tests with Salmonella typhimurium at TMP concentrations of 320 mmole/liter (NIOSH 1983). TMP was carcinogenic in a chronic bioassay with male rats, producing an increased incidence of fibromas of the subcutaneous tissue in the high dose (100 mg/kg) group (National Cancer Institute 1978). However, these results are not considered to be conclusive by expert reviewers of the bioassay results (National Cancer Institute 1978). No tumors occurred in dosed female rats at significantly increased incidences. In the same study, male and female mice were also chronically administered TMP. In male mice no tumors occurred in the dosed groups (250 or 500 mg/kg) at significantly increased incidences. However, in female mice a significant dose-related trend was observed in the incidences of endometrial adenocarcinomas (National Cancer Institute 1978).

Toxicity to Wildlife and Domestic Animals

Schafer et al. (1976) evaluated various chemicals for their potential as chemosterilants in adult male quail (Coturnix c. japonica). At a dose of 75 percent of the oral LD_{50} for quail (750 mg/kg), TMP did not result in a reduced fertility of eggs produced by subsequent matings with untreated females. During the 35 day period after treatment of the male birds, 81 percent of the eggs of their mates were fertile. During days 20-35 post-treatment, 96 percent were fertile.

No data on the aquatic toxicity of TMP or its toxicity to other terrestrial wildlife were located in available literature.

Regulations and Standards

None located.

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

For carcinogenic chemicals the D_T value is most appropriately based on the USEPA Cancer Assessment Group's (CAG) cancer potency slopes. The cancer potency slopes are intended to be a plausible upper bound of the potency of a carcinogen in inducing cancer at low doses. Calculation of a D_T using a cancer potency slope was not possible for TMP because the National Cancer Institute bioassay data have not been quantitatively evaluated using the linearized multistage model (model output data are used by EPA to compute a cancer potency slope). EPA has not evaluated the available carcinogenicity data for TMP and therefore, no weight-of-evidence rating is available for this chemical.

As appropriate cancer potency data are not available for use in computing a D_T value for TMP, data based on non-carcinogenic health effects have been used (recognizing the limitations) to compute an interim D_T value. For TMP, the D_T value is derived from an acute oral toxicity value (LD_{50}) in rats (NIOSH 1983). The D_T value is computed as the product of the acute value and an application factor of 1×10^{-5} (Layton et al. 1986). The application factor allows the derivation of an interim acceptable long-term intake rate (D_T) based on the results of acute tests (LD_{50}) in the absence of more suitable long-term studies (i.e., No-Observed-Effect-Level Studies, NOELs). The application factor corresponds to the cumulative percentile on a

lognormal distribution of NOEL/LD_{50} ratios for various chemicals. The percentile was chosen to reduce the probability that the calculated dose rate would be above a toxic level; the 5th cumulative percentile was used by Layton et al (1986) and was found to be equal to 10^{-3}. The application factor also includes a safety factor of 100 to address interspecies and intraspecies variability; therefore, an interim estimate of D_T is obtained when the application factor is multiplied by the acute value. Because the available data indicate that TMP is carcinogenic in at least one animal species, an additional safety factor of 10 is included in the Layton application factor (i.e., 10^{-6}) to address carcinogenicity. Derivation of this D_T value is as follows:

$$D_T = \text{Acute } LD_{50} \times \text{Application Factor}$$
$$= 840 \text{ mg/kg/day} \times 1 \times 10^{-6}$$
$$= 0.00084 \text{ mg/kg/day}$$

REFERENCES

ADLER, I.D., G. RAMARAO and S.S. EPSTEIN. 1971. In Vivo Cytogenic Effects of Trimethylphosphate and of TEPA on Bone Marrow Cells of Male Rats. Mutat. Res. 13(3):263-273 (Cited in Berkowitz et al. 1978).

BARNARD, P.W.C., C.A. BUNTON, D.R. LLEWELLYN, C.A. VERNON and V.A. WELCH. 1961. The Reactions of Organic Phosphates. Part V. The Hydrolysis of Triphenyl and Trimethyl Phosphates. J. Chem. Soc. 83:2670-76.

BERKOWITZ, J.G., GOYER, M.M., HARRIS, J.C., LYMAN, W.J., HORNE, R.A., NELTEN, L.J. HARRISON, J.E., and ROSENBLATT, D.H. 1978. Literature Review--Problem definition studies on selected chemicals. Final Report. Vol. II. Chemistry, toxicology, and potential environmental effects on selected organic pollutants. Contract No. DAMD 17-77-C-7037, Arthur D. Little, Inc. Cambridge, MA (AD B052946L).

COGLEY, D.R. AND W, FOY. 1978. Readily Available Data on 169 Compounds Associated with Operations at Rocky Mountain and Pine Bluff Arsenals. United States Army Medical Research and Development Command, Ft. Detrick, Frederick, MD. December 1978. AD A074214.

DOMAGE, L. and J. MASSE. 1959. Study of the Hydrolysis of Phosphorus Triesters as a function of pH. Compt. Rend. 249:2209-2211. (Cited in Berkowitz et al. 1978).

EPSTEIN, S.S. W. BASS, E. ARNOLD and Y. BISHOP. 1970. Mutagenicity of Trimethylphosphate in Mice. Science. 168:584-586.

HARBISON, R.D., C. DWIVEDI, and M.A. EVANS. 1976. A Proposed Mechanism for Trimethyl Phosphate-Induced Sterility. Toxicol. Appl. Pharmacol. 35:481-490 (Cited in Berkowitz et al. 1978).

HUDSON, R.F. and D.C. HARPER. 1958. The Reactivity of Esters of Quinquevalent Phosphorus Towards Anions. J. Chem. Soc. 80:1356-1360. (Cited in Berkowitz et al. 1978).

JACKSON, H. and A.R. JONES. 1968. Antifertility Action and Metabolism of Trimethylphosphate in Rodents. Nature. 220:591-592 (Cited in Berkowitz et al. 1978).

JONES, A.R. and H. JACKSON. 1969. Chemosterilant Action of Trimethyl phosphate in Rodents. Brit. J. Pharmacol. 37:531 p. (Cited in Berkowitz et al. 1978).

LAYTON, D.W., MALLOU, B.J., ROSENBLATT, D.H. and SMALL, M.J. 1986. Deriving Allowable Daily Intakes For Systemic Toxicants Lacking Chronic Toxicity Data. Regulatory Toxicology and Pharmacology. In Press.

LEO, A., C. HANSCH and D. ELKINS. 1971. Partition Coefficients and Their Uses. Chem. Rev. 7(6):525 (Cited in Berkowitz et al. 1978).

MCTIGUE, P.T. and P.V. RENOWDEN. 1970. Hydrolysis of Trimethyl Phosphate in Mixed Solvents. Aust. J. Chem. 23:297-306. (Cited in Berkowitz et al. 1978).

NATIONAL CANCER INSTITUTE (NCI). 1978. Bioassay of Trimethylphosphate for Possible Carcinogenicity. U.S. Department of Health, Education and Welfare. NCI-CG-TR-81.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH). 1983. Registry of Toxic Effects of Chemical Substances. Volumes I-III. Department of Health and Human Services. Cincinnati, OH.

OISHI, H., S. OISHI and K. HIRAGA. 1982. Toxicity of Several Phosphoric Acid Esters in Rats. Toxicology Letters. 13:29-34.

SODERMAN, G. 1972. Chromosome Breaking Effect of a Gasoline Additive in Cultured Human Lymphocytes. Hereditas. 71(2):335-338 (Cited in Berkowitz et al. 1978).

TUAZON, E.C., R. ATKINSON, S.M. ASCHMANN, J. AREY, A.M. WINER and J.N. PITTS, JR. 1986. Atmospheric Loss Processes of 1,2-Dibromo-3-Chloropropane and Trimethyl Phosphate. Environ. Sci. Technol. 20(10):1043-1046.

VAN WAZER, J.R. 1961. Phosphorous and its compounds. Volume II. Interscience Publishers, Inc. New York, NY. (Cited in Berkowitz et al. 1978).

WEAST, R.C. (Editor) 1977. CRC Handbook of Chemistry and Physics. 58th Edition. CRC Press Inc., Cleveland, Ohio (Cited in Berkowitz et al. 1978).

VAPONA[1/]

Summary

Vapona is a member of the class of organophosphorus pesticides. The primary mode of toxicity from vapona exposure is through inhibition of the enzyme acetylcholinesterase (ChE). Positive and negative mutagenicity results have been obtained in a variety of test systems. The National Toxicology Program (NTP) is currently undertaking additional studies to assess the mutagenicity and carcinogenicity of vapona.

CAS Number: 62-73-7

Chemical Formula: $(CH_3O)_2P(O)OCH{:}CCl_2$

IUPAC Name: 2,2-Dichlorovinyl dimethyl phosphate

Important Synonyms and Trade Names: Dichlorvos; DDVP

Chemical and Physical Properties

Molecular Weight: 221 (Merck 1983)

Boiling Point: 120°C at 14 mm Hg (Merck 1983)

Specific Gravity: 1.415 (Merck 1983)

Solubility in Water: 10,000 mg/liter (Merck 1983)

1/ Compiled from: United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL). 1985. Physical, Chemical, and Toxicological Data Summaries of 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

Solubility in Organics: Miscible in aromatic hydrocarbon solvents, chlorinated hydrocarbon solvents and alcohol

Log Octanol/Water Partition Coefficient (K_{ow}): 1.4 Hansch and Leo, 1979)

Soil/Water Partition Coefficient (K_{oc}):

28	Lyman et al. (1982) Eqn 4-5 (S = 10,000)
138	Lyman et al. (1982) Eqn 4-8 (log K_{ow} = 1.4)
36	Lyman and Loreti (1986) Eqn I (log K_{ow} = 1.4)
29	Lyman and Loreti (1986) Eqn II (log K_{ow} = 1.4)
30	Lyman and Loreti (1986) Eqn III (log K_{ow} = 1.4)
64	Kadeg et al. (1986) (log K_{ow} = 1.4)

Bioconcentration Factor:

6.8	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 1.4)
3.4	Davies and Dobbs (1984) Eqn A (S = 10,000)
7.6	Davies and Dobbs (1984) Eqn C (log K_{ow} = 1.4)
11	Davies and Dobbs (1984) Eqn B (log K_{ow} = 1.4)

Vapor Pressure: 1.2×10^{-2} mm Hg at 20°C (Merck 1983)

Henry's Law Constant: 2.0×10^{-7} atm-m^3/mole (calculated)
2.9×10^{-7} atm-m^3/mole (calculated)

Transport and Fate

The vapor pressure of vapona suggests that some volatilization from environmental media is likely to occur. It is possible that released vapona vapors will hydrolyze following reactions with atmospheric moisture and result in hydrolysis products such as desmethyl dichlorvos. At acidic pHs, vapona is more stable (i.e., more resistant to hydrolysis). For example, at 38°C and pHs of 1 or 9, the respective half-lives of vapona are 50 and 4.5 hours (TBD Peer Review Committee 1984). At 37.5°C and neutral pH (pH = 7) the half-life was 28 hours. The likely primary hydrolysis product--desmethyl dichlorvos--may further hydrolyze to chlorofenvinphos (Supona) (USAMBRDL 1985). Cogley and Foy (1978) indicate a half-life of less than one month for vapona.

A range of estimated soil/water partition coefficients (K_{oc}) is reported above and indicates that some sorption of vapona to soils/sediments and dissolved organic material will occur. The combined water solubility and low organic partitioning suggest that vapona will exhibit some degree of environmental mobility.

A range of estimated bioconcentration factors (BCFs) is also reported above. ASTM (1985) indicates that chemicals with bioconcentration factors less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the concentration factors suggests that appreciable bioconcentration or biomagnification of vapona residues is not likely to occur.

Health Effects

The primary mode of toxicity of vapona in humans and animals is through inhibition of the enzyme acetylcholinesterase (ChE) in the central and peripheral nervous systems. Symptoms of exposure include headache, blurred vision, constricted pupils, chest tightness, salivation, sweating, muscular weakness, tremors, and convulsions with death occurring (at very high doses) from respiratory failure (Shell Internationale, 1981). Men exposed for 30-60 minutes to vapona concentrations up to 6.9 mg/m^3 exhibited no clinical effects or inhibition of blood ChE activity (Shell Internationale 1981). Groups of five men received total oral doses of 1.0, 1.5, 2.0, or 2.5 mg/day vapona divided over two gelatin capsules for 28 days. Another group received 1.5 mg/day for 60 days. The 2.5 mg/day dose groups experienced decreases in plasma ChE activity beginning the second week. When plasma ChE levels showed a 30 percent decrease (20 days) the dosing was discontinued. The 2.0 mg/day dose also produced a reduction in plasma ChE during the second week of dosing, which reached a maximum of 29 percent two days following the last dose. The 1.5 mg/day dose group (28 day exposure) exhibited no change in plasma ChE, while those in the 60 day study exhibited reduced plasma ChE (27 percent). The 1.0 mg/day group also exhibited no change in plasma ChE levels.

A subchronic oral toxicity study in rats exposed to diets containing 0, 5, 20, 200, 500, or 1,000 ppm vapona resulted in decreased plasma ChE activity at all dose levels as compared with controls. Levels of ChE gradually returned to normal levels except in the 200 ppm and higher dose groups. Erythrocyte ChE was also decreased in the 200 ppm and higher dose groups (Shell Internationale, 1981). In another study, rats fed vapona for 15 weeks in their diet (0, 0.1, 1.0, 10, 100, or 1,000 ppm) displayed no signs of toxicity. Rats in the highest dose group exhibited decreased growth rates at the beginning of the study and marked inhibition of ChE activity in plasma, erythrocytes and brains. Females in the 10 and 100 ppm groups also displayed reduced levels of plasma and erythrocyte ChE activity (Shell Internationale, 1981).

Rats chronically exposed (2 years) to 0.047, 4.67, 46.7, or 234 ppm vapona displayed no signs of intoxication. No effects were observed on behavior, mortality rate, weight gain, food consumption, terminal body and organ weights, hematology, urinalysis, or tumor incidence (Shell Internationale 1981). Plasma and erythrocyte ChE were depressed throughout the study in the two high dose groups. Brain ChE activity was depressed only in the highest group. Histological examination revealed hepatocellular vacuolization in the high dose group and in most females and some males at 46.7 ppm. The identified No-Observed-Effect-Level (NOEL) in this study was 4.7 ppm. No carcinogenic effects were noted in the study (Shell Internationale 1981). In another chronic study, dogs exposed to vapona in their diets (0.09, 0.32, 3.2, 32.0 or 256 ppm) exhibited no differences in survival, weight gain, food consumption, hematology, or urinalysis. Plasma ChE was decreased at the two highest doses and erythrocyte ChE activity was depressed at 3.2 ppm and above. It was concluded that 0.32 ppm was the NOEL for this study.

Positive indications of mutagenicity have been observed following vapona treatment in Aspergillus nidulans (point mutations, cross-overs); Chinese hamster fibroblast lung cells (breaks, translocations, rings, gaps); and Chinese hamster V79 cells (sister chromatid exchange) (Shell International 1981). Positive results were

also obtained by the NTP with L5178Y mouse lymphoma cells (NTP 1985). Vapona has also tested positive for cytogenetic effects in Chinese hamster ovary cells (NTP 1986). Negative results were obtained following vapona treatment in Drosophila melanogaster (Shell International 1981). Dominant lethal assays in mice, cytogenetic studies on bone marrow and spermatogonia in mice and Chinese hamsters as well as host-mediated assays have all been negative (Shell Internationale 1981). Vapona has been selected by the National Toxicology Program (NTP) for mutagenicity testing in Salmonella. Vapona is currently in the chronic phase of toxicology and carcinogenesis studies which are being undertaken by the NTP (NTP 1985).

No teratogenic effects were observed following vapona exposure in rabbits during days 6-18 of gestation; nor in rats or mice dosed during gestation (Shell International 1981). No reproductive effects were noted in a three generation study in rats fed 0.1, 1.0, 10, 100, or 500 ppm vapona. However, rabbits given 5 mg/kg orally during days 6-18 of gestation exhibited an increased number of resorptions (USAMBRDL 1985).

The acute oral toxicity values (LD_{50}) for vapona in male and female rats are 80 mg/kg and 56 mg/kg, respectively (USAMBRDL 1985).

Toxicity to Wildlife and Domestic Animals

Cows fed grain which contained 20 ppm vapona for eight days exhibited no signs of toxicity or depression of ChE activity (Shell Chemical Company 1965). However, at concentrations of 100 and 200 ppm a slight depression of erythrocyte ChE was observed after eight days, while at 500 and 2,000 ppm severe depression of erythrocyte ChE was observed at eight days (Shell Chemical Company 1965).

Acute toxicity data is available for avian species. Acute oral LD_{50} values for pheasants (Phasianus colchicus), mallard ducks (Anas platyrhynchos), starlings (Sturnus vulgaris), and redwing blackbirds (Anglaius phoeniceus), are 9.0 mg/kg, 7.8 mg/kg, 12 mg/kg, and 17 mg/kg, respectively (Shell Internationale 1981).

The acute toxicity of vapona to freshwater fish has been evaluated. The 96 hr LC_{50} values for cutthroat trout (Salmo clarki), lake trout (Salvelinus namaycush), bluegills (Lepomis macrochirus) and fathead minnows (Pimephales promelas) are 0.17 mg/l, 0.19 mg/l, 0.9 mg/l and 12 mg/l, respectively (Shell Internationale, 1981).

The acute oral toxicity of vapona (LD_{50}) in rabbits is 12.5 mg/kg and approximately 100-300 mg/kg in the dog (USAMBRDL 1985).

Regulations and Standards

OSHA Threshold Limit Value: TWA[1/] = 1 mg/m^3 (skin)
ACGIH Threshold Limit Value: 0.1 ppm

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

For vapona, the D_T value is based on a chronic (2 year) oral toxicity study utilizing dogs fed concentrations of 0.09, 3.2, 32, or 256 ppm vapona in their diets (Shell Internationale 1981). Inhibition of ChE activity was the primary endpoint of concern, though other parameters such as weight gain, food consumption, survival and hematology were also examined. The No-Observed-Effect-Level (NOEL) for vapona identified from this study was 0.32 ppm (0.008 mg/kg/day). An Uncertainty Factor of 100 is utilized in computing the D_T value to address the extrapolation of results to humans (10) and to protect sensitive subgroups (intraspecies variability) (10). Derivation of the D_T for vapona is as follows:

1/ Time Weighted Average

$$D_T = \frac{NOEL}{UF} \text{ (mg/kg/day)}$$

$$= \frac{0.008}{100}$$

$$= 0.00008 \text{ mg/kg/day}$$

Though a number of short-term studies in humans are available, the D_T value was instead based on the available chronic data for dogs as this species appeared more sensitive. In using the chronic dog No-Observed-Effect-Level (NOEL) the computed D_T becomes more protective and appears to be justified if one assumes that humans are at least as sensitive as dogs to long term (chronic) vapona exposures.

References

ASTM. 1985. Standard Practice for conducting bioconcentration tests with fishes and saltwater bivalve mollusca. Designation E 1022-84, pages 590-62. In: 1985 Annual Book of ASTM Standards Volume 11.04. American Society for Testing and Materials, Philadelphia, Pennsylvania.

COGLEY, D.R. AND FOY, W. 1978. Readily Available Data on 169 Compounds Associated with Operations at Rocky Mountain and Pine Bluff Arsenals. United States Army Medical Research and Development Command, Ft. Detrick, Frederick, MD. December 1978. AD A074214.

DAVIES, R.P. and A.J. DOBBS. 1984. The prediction of bioconcentration in fish. Water Res. 18(10):1253-1262.

HANSCH, C. and A.J. LEO. 1979. Substituent constants for correlation analysis in chemistry and biology. John Wiley and Sons, New York, NY.

KADEG, R.D., PAVLOU, S.P., DUXBURY, A.S. 1986. Elaboration of Sediment Normalization Theory for Non Polar Hydrophobic Organic Chemicals. U.S. Environmental Protection Agency, Criteria and Standards Division, Washington D.C.

LYMAN, W.J., LORETI, C.P. 1986. Prediction of Soil and Sediment Sorption for Organic Compounds (Comment Final Draft). U.S. Environmental Protection Agency, Monitoring and Data Support Division, Office of Water Regulations and Standards. Washington D.C.

LYMAN, W.J., W.F. REEHL AND D.H. ROSENBLATT. 1982. Handbook of Chemical Property Estimation Methods: Environmental Behavior of Organic Compounds. McGraw-Hill Book Co., New York, NY.

NATIONAL TOXICOLOGY PROGRAM (NTP). 1985. Fiscal Year 1985 Annual Plan. U.S. Department of Health and Human Services. Washington, D.C.

SHELL CHEMICAL COMPANY. 1965. Summary of Toxicology and Pharmacology of Dichlorvos (Vapona^{R} Insecticide). Technical Report No. SM-262-65.

SHELL INTERNATIONALE. 1981. Group Toxicology Division. Review of Toxicology. Dichlorvos. Review Series Tox 81-001 (Proprietary Information), Shell International Research Maatschappij V.B., The Hague, Netherlands.

TBD PEER REVIEW COMMITTEE. 1984. Toxicology Data Bank, National Library of Medicine and National Institutes of Health. Department of Health and Human Services, Washington, D.C. (Computerized Data Base).

THE MERCK INDEX. 1983. An Encyclopedia of Chemicals, Drugs and Biologicals. Tenth ed. Windholz, M., Budavan, S., Blumetti, R.F. and Otterbein, E.S. (eds.). Merck and Company, Inc., Rahway, New Jersey.

UNITED STATES ARMY MEDICAL BIOENGINEERING RESEARCH AND DEVELOPMENT LABORATORY (USAMBRDL). 1985. Physical, Chemical, and Toxicological Data Summaries of 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

XYLENES (o,m,p)[1/]

Summary

Xylene has been shown to be fetotoxic in rats and mice. In humans, exposure to high concentrations of xylene adversely affects the central nervous system and irritates the mucous membranes. Prolonged exposure to high concentrations can cause severe lung congestion and intra-alveolar hemorrhage.

Xylene has three isomers, o-, m-, and p-xylene. They generally have similar chemical and biological characteristics and therefore will be discussed together.

CAS Number:

Mixed:	1330-20-7
m-Xylene:	109-38-3
o-Xylene:	95-47-6
p-Xylene:	106-42-3

Chemical Formula: $C_6H_4(CH_3)_2$

IUPAC Name: Dimethylbenzene

Important Synonyms and Trade Names:

Mixed xylene:	Dimethylbenzene, xylol
m-Xylene:	1,3-Dimethylbenzene, m-xylol
o-Xylene:	1,2-Dimethylbenzene, o-xylol
p-Xylene:	1,4-Dimethylbenzene, p-xylol

1/ Compiled from: U.S. Environmental Protection Agency, Office of Waste Program Enforcement. September 1985. Chemical, physical, and biological properties of compounds present at hazardous waste sites. A Final Report Prepared by Clement Associates, Inc., Arlington, Virginia.

Also: United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL). 1985. Physical, Chemical, and Toxicological Data Summaries of 62 Compounds Present at Rocky Mountain Arsenal. USAMBRDL. Fort Detrick, Frederick, MD.

Chemical and Physical Properties

Molecular Weight: 106.17

Boiling Point: Mixed: 137-140°C
m-Xylene: 139°C
o-Xylene: 144°C
p-Xylene: 138°C

Melting Point: m-Xylene: -48°C
o-Xylene: -25°C
p-Xylene: 13°C

Specific Gravity: 0.86

Solubility in Water: 130 mg/liter at 25°C [m-xylene] (USEPA 1985a)
175 mg/liter at 25°C [o-xylene] (Sax 1986)
198 mg/liter at 25°C [p-xylene] (Sax 1986)

Solubility in Organics: Soluble in alcohol, ether, and other organic solvents

Log Octanol/Water Partition Coefficient (K_{ow}):

o-xylene: 2.77 (Moriguchi 1975)
2.95 (Valvani et al. 1980)
3.13 (Tewari et al. 1982) Table I
p-xylene: 3.15 (Valvani et al. 1980; Moriguchi 1975)
3.18 (Tewari et al. 1982)
m-xylene: 3.20 (Valvani et al. 1980; Tewari et al. 1982; Moriguchi 1975)

Soil/Water Partition Coefficient (K_{oc}):

[o, p, m isomers:]

765; 1,157; 1,312	Lyman et al. (1982) Eqn 4-5 (log K_{ow} = 2.77, 3.1, 3.2)
415; 750; 897	Lyman and Loreti (1986) Eqn I (log K_{ow} = 2.77, 3.1, 3.2)
405; 763; 924	Lyman and Loreti (1986) Eqn II (log K_{ow} = 2.77, 3.1, 3.2)
408; 763; 922	Lyman and Loreti (1986) Eqn III (log K_{ow} = 2.77, 3.1, 3.2)
614; 1,059; 1,249	Kadeg et al. (1986) (log K_{ow} = 2.77, 3.1, 3.2)

Bioconcentration Factor:

95	Davies and Dobbs (1984) Eqn B (log K_{ow} = 3)
56	Davies and Dobbs (1984) Eqn C (log K_{ow} = 3)
34.7	Davies and Dobbs (1984) Eqn A (S = 165)[1/]
75	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 2.77)
134	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 3.10)
146	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 3.15)
159	Lyman et al. (1982) Eqn 5-2 (log K_{ow} = 3.20)
8.7	Davies and Dobbs (1984) Eqn A (log K_{ow} = 3.10)
109	Davies and Dobbs (1984) Eqn B (log K_{ow} = 3.10)
51.4	Davies and Dobbs (1984) Eqn C (log K_{ow} = 3.10)

Vapor Pressure: 10 mm Hg at 25°C

Vapor Density: 3.7

Flash Point 25°C (closed cup)

Henry's Law Constant: 5.6×10^{-4} atm-m^3/mole (calculated)
7.04×10^{-3} atm-m^3/mole (USEPA 1985a)

Transport and Fate

Volatilization and subsequent photooxidation by reaction with hydroxyl radicals in the atmosphere are important transport and fate processes for xylene occurring in the upper layer of soil and in aquatic environments. Products of the hydroxylation reaction include carbon dioxide, peroxyacetylnitrate (PAN), and cresol. A range of estimated soil-water partition coefficients (K_{OC}) is reported above and indicates that sorption of xylenes to soil/sediment and dissolved organic material will occur. Pavlou (1980) estimates that sorption of volatile organics will range from low to moderate. The combined water solubility and organic partitioning indicate that xylene and its isomers will exhibit some degree of environmental mobility. Biodegradation is also an important fate process in both soils and the

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1/ Geometric mean of the three isomer solubilities is used in this equation.

aquatic environment. Xylenes have been shown to persist for up to 6 months in soil. Because of their low water solubility high octanol/water partition coefficient and rapid biodegradation, xylenes are unlikely to leach rapidly into groundwater in high concentrations.

A range of estimated bioconcentration factors (BCFs) for xylenes is also reported above. ASTM (1985) indicates that chemicals with bioconcentration factors less than approximately 100 have low potential for causing harm to wildlife and human health via biomagnification of residues up food chains. The magnitude of the concentration factors suggests that some bioconcentration of xylene residues may occur.

Health Effects

The National Toxicology Program (NTP) has recently conducted oral toxicity tests with mixed xylenes in rats and mice to determine carcinogenicity. Groups of 50 rats of each sex were administered doses of 0, 250, or 500 mg/kg xylenes by gavage 5 days/week for 103 weeks in a carcinogenicity test (NTP 1986). Groups of 50 mice of each sex were administered 0, 500, or 1,000 mg/kg xylenes on the same schedule. At no site was the incidence of nonneoplastic or neoplastic lesions in dosed rats or mice of either sex considered to be related to the administration of xylenes (NTP 1986). Survival rates of male rats was dose related (e.g., vehicle control survival, 36/50; low dose, 26/50 and high dose 20/50). Most of the deaths were gavage related. Body weights of high dose males were slightly lower (5-8 percent) than those of controls after week 59. Mean body weights of low dose and control male rats and dosed (all levels) and control female rats were comparable. Survival rates of female rats and both sexes of dosed mice were not significantly different from controls. Mixed xylenes (o, m, p-xylene or ethylbenzene) were not mutagenic when tested with or without metabolic activation in several Salmonella typhimurium strains (NTP 1986).

Xylene is not teratogenic but has caused fetotoxicity in exposed rats and mice. Acute exposure to high levels of xylene affects the central nervous system and irritates the mucous membranes. Aged rats were exposed to a single concentration of xylene (200 ppm) in their diets for up to six months in a study by Bowers et al. (1982). No gross or light microscopic effects were seen. The administered concentration was considered a No-Observed-Adverse-Effect-Level (NOAEL) because ultrastructural changes in liver morphology which did not appear to be adverse were noted (USEPA 1984). Weaknesses of the study include: the use of aged animals, a lack of chemical stability monitoring, the use of a single exposure level and a lack of examination of other tissues. The oral LD_{50} value of xylene in rats is 4,300 mg/kg (NIOSH 1983). The inhalation LC_{50} value (4 hr) in rats is 5,000 ppm (NIOSH 1983).

Toxicity to Wildlife and Domestic Animals

Xylene adversely affected adult trout at concentrations as low as 3.6 mg/liter in a continuous flow system. Juvenile trout avoided xylene at concentrations greater than 0.1 mg/liter. The LC_{50} in adult trout was determined to be 13.5 mg/liter. The LC_{50} values for other freshwater fish were approximately 30 mg/liter in a static system [Note: This test likely underestimated toxicity because the concentration in the water column available for uptake, is not constant]. Only a few studies have been done on the toxicity of xylene to saltwater species. These indicated that the m- and o-xylene isomers have similar toxicities and are probably less toxic than p-xylene, and that saltwater species are generally more susceptible than freshwater species to the detrimental effects of xylene (LC_{50} = 10 mg/liter for m- and o-xylene and LC_{50} = 2 mg/liter for p-xylene). However, these generalizations are based on limited data.

No information on the toxicity of xylenes to terrestrial wildlife and domestic animals was available in the literature reviewed. However, because of the low acute toxicity of xylenes and the high volalility it is unlikely that they would be encountered in concentrations which would be toxic to wild or domestic birds or mammals.

Regulations and Standards

NIOSH Recommended Standards (air): TWA[1/] = 435 mg/m^3
Ceiling Level = 870 mg/m^3 (10 min)

OSHA Standard (air) = TWA: 435 mg/m^3

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

For xylenes the D_T value is derived from the data used to establish an EPA proposed Drinking Water Recommended Maximum Contaminant Level (RMCL) (50 Federal Register 47008 Wednesday November 13, 1985. See also: USEPA 1985b). For xylenes (o,m,p isomers), the RMCL is based on an inhalation study using rats, guinea pigs, monkeys and dogs exposed continuously to concentrations of 337 mg/m^3 o-xylene for a period of 90 days (Jenkins et al. 1970). No significant effects were observed with respect to body weight, hematology or histopathology. The No-Observed-Adverse-Effect-Level (NOAEL) identified from this study was 337 mg/m^3. The total absorbed dose for a human was computed from the exposure concentration, an average breathing rate, an absorption factor for o,m,p-xylenes (Sedivek and Flek 1976) and the body weight of a reference human as follows:

$$\text{Absorbed dose} = \frac{(337 \text{ mg/m}^3)(20 \text{ m}^3\text{/day})\ (0.64)}{70 \text{ kg}}$$

$$= 61.62 \text{ mg/kg/day}$$

1/ Time Weighted Average.

An Uncertainty Factor of 1,000 is employed in computing the D_T to address the extrapolation of results to humans (10), intraspecies variability (sensitive subgroups) (10), and the use of subchronic rather than chronic toxicity data (10). Derivation of the D_T value is as follows:

$$D_T = \frac{\text{Absorbed Dose}}{UF}$$

$$= \frac{61.62}{1,000}$$

$$= 0.062 \text{ mg/kg/day}$$

REFERENCES

ASTM. 1985. Standard Practice for conducting bioconcentration tests with fishes and saltwater bivalve mollusca. Designation E 1022-84, pages 590-62. In: 1985 Annual Book of ASTM Standards Volume 11.04. American Society for Testing and Materials, Philadelphia, Pennsylvania.

BOWERS, D.E., JR., M.S. CANNON and D.H. JONES. 1982. Ultrastructural changes in livers of young and aging rats exposed to methylated benzenes. Am. J. Vet. Res. 43(4): 679-683

DAVIES, R.P. and A.J. DOBBS. 1984. The prediction of bioconcentration in fish. Water Res. 18(10):1253-1262.

JENKINS, L.J., R.A. JONES and J. SIEGEL. 1970. Long-term inhalation screening studies of benzene, toluene, o-xylene and cumene on experimental animals. Toxicol. Appl. Pharmacol. 16:818-823.

KADEG, R.D., PAVLOU, S.P., DUXBURY, A.S. 1986. Elaboration of Sediment Normalization Theory for Non Polar Hydrophobic Organic Chemicals. U.S. Environmental Protection Agency, Criteria and Standards Division, Washington D.C.

LYMAN, W.J., LORETI, C.P. 1986. Prediction of Soil and Sediment Sorption for Organic Compounds (Comment Final Draft). U.S. Environmental Protection Agency, Monitoring and Data Support Division, Office of Water Regulations and Standards. Washington D.C.

LYMAN, W.J., REEHL, W.F., and ROSENBLATT, D.H. 1982. Handbook of Chemical Property Estimation Methods: Environmental Behavior of Organic Compounds. McGraw-Hill Book Co., New York.

MORIGUCHI, I. 1975. Quantitative structure-activity studies: I. Parameters relating to hydrophobicity. Chem. and Pharm. Bull. 23(2): 247-257.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH). 1983. Registry of Toxic Effects of Chemical Substances. Data Base. Washington D.C. October 1983.

NATIONAL RESEARCH COUNCIL (NRC). 1980. The Alkyl Benzenes. National Academy Press, Washington, D.C.

NATIONAL TOXICOLOGY PROGRAM (NTP). 1986. Toxicology and carcinogenesis studies of xylenes (mixed) (60 percent m-xylene, 14 percent p-xylene, 9 percent o-xylene, and 17 percent ethylbenzene) in F344/N rats and B6C3F$_1$ Mice (Gavage Studies). U.S. Department of Health and Human Services. Public Health Service, National Institute of Health. Technical Report Series No. 327.

PAVLOU, S.P. 1980. Thermodynamic Aspects of Equilibrium Sorption of Persistent Organic Molecules at the Sediment-Seawater Interface: A Framework For Predicting Distributions in the Aquatic Environment. IN: Contaminants and Sediments. Volume 2. Baker, R.A. (Editor). Science Publishers, Inc. Ann Arbor, MI.

SAX, I.N. (EDITOR). 1986. Hazardous Chemicals Information Annual, No. 1. Van Nostrand Rienhold, New York. 766 pp.

SEDIVEC, V. and FLEK, J. 1976. The absorption, metabolism and excretion of xylenes in man. Int. Arch. Occup. Environ. Health. 37:205-217.

TEWARI, Y.B., M.M. MILLER, S.P. WASIK, and MARTIRE, D.E. 1982. Aqueous solubility and octanol-water partition coefficient of organic compounds at 25°C. J. Chem. Eng. Data.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1978. Initial Report of the TSCA Interagency Testing Committee to the Administrator, Environmental Protection Agency. January 1978. EPA 560-10-78/001.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1979. Water-Related Environmental Fate of 129 Priority Pollutants. Washington D.C. December 1979. EPA 440/4-79-029.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1984. Health Effects Assessment for Xylene. Final Draft. Environmental Criteria and Assessment Office, Cincinnati, Ohio. September 1984. ECAO-CIN-H006.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1985a. Draft Superfund Public Health Evaluation Manual. Prepared by: ICF Incorporated, Washington D.C. USEPA Office of Solid Waste and Emergency Response, Washington D.C. EPA Contract No. 68-01-7090.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1985b. Draft Health Advisory. Xylenes. Office of Drinking Water USEPA. Washington, D.C. September 30, 1985.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1986. Quality Criteria for Water, 1986 ("The Gold Book"). Office of Water Regulations and Standards, Washington, DC. EPA 440/5-86-001.

VALVANI, S.C., YALKOWSKY, S.H., and ROSEMAN, T.J. 1980. Solubility and partitioning. IV. Aqueous solubility and octanol-water partition coefficients of liquid nonelectrolytes. J. Pharm. Sci. 70 (5):502-202.

VERSCHUEREN, K. 1977. Handbook of Environmental Data on Organic Chemicals. Van Nostrand Reinhold Co., New York. 659 pages.

WEAST, R.E., ed. 1981. Handbook of Chemistry and Physics. 62nd ed. CRC Press, Cleveland, Ohio. 2,332 pages.

ZINC[1/]

Summary

Ingestion of excessive amounts of zinc can cause fever, vomiting, and stomach cramps. Exposure to high concentrations of zinc oxide fumes can cause metal fume fever. Inhalation of mists or fumes may irritate the respiratory tract, and contact with zinc chloride may irritate the eyes and skin. High levels of zinc in the diet have been shown to retard growth and produce defective mineralization of bone. Zinc generally exists in nature as a salt with a valence of $^{+}2$.

CAS Number: 7440-66-6

Chemical Formula: Zn

IUPAC Name: Zinc

Chemical and Physical Properties

Atomic Weight: 65.38

Boiling Point: 907°C

Melting Point: 419.58°C

Specific Gravity: 7.133 at 25°C

Solubility in Water: Insoluble; some salts are soluble

1/ Compiled from: U.S. Environmental Protection Agency, Office of Waste Program Enforcement. September 1985. Chemical, physical, and biological properties of compounds present at hazardous waste sites. A Final Report Prepared by Clement Associates, Inc., Arlington, Virginia.

Solubility in Organics: Soluble in acid and alkali

Vapor Pressure: 1 mm Hg at 487°C

Transport and Fate

Zinc can occur in both suspended and dissolved forms. Dissolved zinc may occur as the free (hydrated) zinc ion or as dissolved complexes and compounds with varying degrees of stability and toxicity. Suspended (undissolved) zinc may be dissolved following minor changes in water chemistry or may be sorbed to suspended matter. The predominant fate of zinc in aerobic aquatic systems is sorption of the divalent cation by hydrous iron and manganese oxides, clay minerals, and organic material. The efficiency of these materials in removing zinc from solution varies according to their compositions and concentrations, the pH and salinity of the water, the concentrations of complexing ligands, and the concentration of zinc. Concentrations of zinc in suspended and bed sediments always exceed concentrations in ambient water. In reducing environments, precipitation of zinc sulfide limits the mobility of zinc. However, under aerobic conditions, precipitation of zinc compounds is probably important only where zinc is present in high concentrations. Zinc tends to be more readily sorbed at higher pH than lower pH and tends to be desorbed from sediments as salinity increases. Compounds of zinc with the common ligands of surface waters are soluble in most neutral and acidic solutions, so that zinc is readily transported in most unpolluted, relatively organic-free waters.

The relative mobility of zinc in soil is determined by the same factors affecting its transportation in aquatic systems. Atmospheric transport of zinc is also possible. However, except near sources such as smelters, zinc concentrations in air are relatively low and fairly constant.

Since it is an essential nutrient, zinc is bioaccumulated even in the absence of abnormally high ambient concentrations. Zinc does not appear to be biomagnified. Although zinc is actively bioaccumulated in aquatic systems, the biota appear to represent a relatively minor sink compared to the sediments. Zinc is one of the most important metals in biological systems. Since it is actively bioaccumulated, the environmental concentrations of zinc probably exhibit seasonal fluctuations.

Health Effects

Testicular tumors have been produced in rats and chickens when zinc salts are injected intratesticularly, but not when other routes of administration are used (USEPA 1984). Zinc may be indirectly important with regard to cancer since its presence seems to be necessary for the growth of tumors. Laboratory studies suggest that although zinc-deficient animals may be more susceptible to chemical induction of cancer, tumor growth is slower in these animals (USEPA 1984). There is no evidence that zinc deficiency has any etiological role in human cancer. There are no data available to suggest that zinc is mutagenic or teratogenic in animals or humans (USEPA 1984).

Zinc is an essential trace element that is involved in enzyme functions, protein synthesis, and carbohydrate metabolism (USEPA 1984). Ingestion of excessive amounts of zinc may cause fever, vomiting, stomach cramps, and diarrhea. Fumes of freshly formed zinc oxide can penetrate deep into the alveoli and cause metal fume fever (USEPA 1984). Zinc oxide dust does not produce this disorder. Contact with zinc chloride can cause skin and eye irritation. Inhalation of mists or fumes may irritate the respiratory and gastrointestinal tracts. Zinc in excess of 0.25 percent in the diet of rats causes retardation, hypochromic anemia, and defective mineralization of bone (USEPA 1984). No zinc toxicity is observed at dietary levels below 0.25 percent.

Studies with animals and humans indicate that metabolic changes may occur due to the interaction of zinc and other metals in the diet. Exposure to cadmium can cause changes in the distribution of zinc, with increases in the liver and kidneys, organs where cadmium also accumulates. Excessive intake of zinc may cause copper deficiencies and result in anemia. Interaction of zinc with iron or lead may also lead to changes that are not produced when the metals are ingested individually.

Toxicity to Wildlife and Domestic Animals

Zinc produces acute toxicity in freshwater organisms over a range of concentrations from 90 to 58,100 µg/liter and appears to be less toxic in harder water (USEPA 1980). Acute toxicity is similar for freshwater fish and invertebrates (USEPA 1980). Chronic toxicity values range from 47 to 852 µg/liter and appear to be relatively unaffected by hardness (USEPA 1980). A final acute-chronic ratio for freshwater species of 3.0 has been reported. Although most freshwater plants appear to be insensitive to zinc, one species, the alga Selenastrum capricornutum, exhibited toxic effects at concentrations from 30 to 700 µg/liter (USEPA 1980). Reported acute toxicity values range from 2,730 to 83,000 µg/liter for saltwater fish and from 166 to 55,000 µg/liter for invertebrate saltwater species (USEPA 1980). Zinc produces chronic toxicity in the mysid shrimp at 166 µg/liter. The final acute-chronic ratio for saltwater species is 3.0. Toxic effects are observed in saltwater plant species at zinc concentrations of 50 to 25,000 µg/liter (USEPA 1980).

Zinc poisoning has occurred in cattle. In one outbreak, poisoning was caused by food accidentally contaminated with zinc at a concentration of 20 g/kg. An estimated intake of 140 g of zinc per cow per day for about 2 days was reported. The exposed cows exhibited severe arthritis, and some died or had to be slaughtered. Postmortem findings showed severe pulmonary emphysema with changes in the myocardium, kidneys, and liver. Zinc concentrations in the liver were extremely high. Based on relatively limited data, some researchers

have speculated that exposure to excessive amounts of zinc may constitute a hazard to horses. Laboratory studies and findings in foals living near lead-zinc smelters suggest that excessive exposure to zinc may produce bone changes, joint afflictions, and lameness. In pigs given dietary zinc at concentrations greater than 1,000 mg/kg, decreased food intake and weight gain were observed. At dietary levels greater than 2,000 mg/kg, deaths occurred as soon as 2 weeks after exposure; severe gastrointestinal changes and brain damage, both of which were accompanied by hemorrhages, were observed, as well as changes in the joints. High concentrations of zinc were found in the liver in these same studies.

Regulations and Standards

Ambient Water Quality Criteria (USEPA 1986):

Aquatic Life (Freshwater)

Acute toxicity: $e^{(0.83[\ln (\text{hardness})] + 1.95)}$ µg/liter
Chronic toxicity: 47 µg/liter

At hardnesses of 50, 100, and 200 mg/liter $CaCO_3$, the acute criteria are 180, 320 and 570 µg/liter.

Aquatic Life (Saltwater)

Acute toxicity: 170 µg/liter
Chronic toxicity: 58 µg/liter

Human Health

Organoleptic criterion: 5 mg/liter

NIOSH Recommended Standard: 5 mg/m^3 (zinc oxide)

OSHA Standard: TWA[1/] = 5 mg/m^3 (zinc oxide)

ACGIH Threshold Limit Values:

Zinc chloride fume:	TWA = 1 mg/m^3	
	STEL[2/] = 2 mg/m^3	
Zinc oxide fume:	TWA = 5 mg/m^3	
	STEL = 10 mg/m^3	
Zinc oxide dust:	TWA = 10 mg/m^3	(nuisance particulate)
Zinc stearate:	TWA = 10 mg/m^3	(nuisance particulate)
	STEL = 20 mg/m^3	

D_T Value

The D_T value is defined as that contaminant intake rate (mg/kg/day) that should not induce an adverse effect to human health or should not pose a risk of cancer occurrence greater than a predetermined risk level.

The D_T value for zinc is based on the same data used by EPA to generate the acceptable chronic intake value for oral exposure (USEPA 1984). The human data which have been used as a basis for this value are case reports of the therapeutic use of zinc to accelerate the healing of ulcers, arthritis and to aid recovery of sickle cell anemia patients. Oral dosages of encapsulated zinc approximating a total daily dose of 150 mg/day were administered (2.14 mg/kg/day assuming a 70 kg human weight). No adverse effects were noted. Therefore, this dose was chosen as a human median effective dose (MED) from which to derive an acceptable oral chronic intake. An Uncertainty Factor (UF) of 10 is employed to protect sensitive human populations. Derivation of the D_T for zinc is computed as follows:

1/ Time Weighted Average
2/ Short Term Effect Level

$$D_T = \frac{\text{MED (mg/kg/day)}}{UF}$$

$$= \frac{2.14}{10}$$

$$= 0.214 \text{ mg/kg/day}$$

REFERENCES

AMERICAN CONFERENCE OF GOVERNMENTAL INDUSTRIAL HYGIENISTS (ACGIH). 1980. Documentation of the Threshold Limit Values. 4th ed. Cincinnati, Ohio. 488 pages.

CASARETT, L.J., and DOULL, J., eds. 1975. Toxicology: The Basic Science of Poisons. Macmillan Publishing Co., New York. 768 pages.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH). 1983. Registry of Toxic Effects of Chemical Substances. Data Base. Washington, D.C.. October 1983.

SAX, N.I. 1975. Dangerous Properties of Industrial Materials. 4th Ed. Van Nostrand Reinhold Co., New York. 1,258 pages.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1979. Water-Related Environmental Fate of 129 Priority Pollutants. Washington, D.C. December 1979. EPA 440/4-79-029.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1980. Ambient Water Quality Criteria for Zinc. Office of Water Quality and Standards, Criteria and Standards Division, Washington, D.C. October 1980. EPA 440/5-80-079.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1984. Health Effects Assessment for Zinc. Final Draft. Environmental Criteria and Assessment Office, Cincinnati, Ohio. September 1984. ECAO-CIN-H048.

WEAST, R.E., ed. 1981. Handbook of Chemistry and Physics. 62nd ed. CRC Press, Cleveland, Ohio. 2,332 pages.